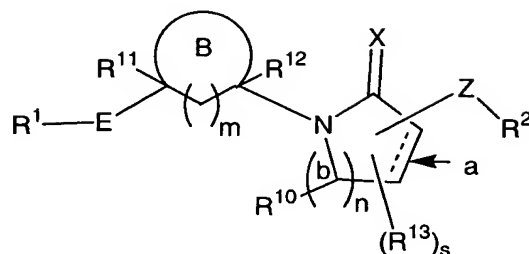


## Claims:

1. A compound of formula (I):



(I)

or a stereoisomer or a pharmaceutically acceptable salt thereof, wherein:

- 10 ring B is a cycloalkyl group of 3 to 8 carbon atoms wherein the cycloalkyl group is saturated or partially unsaturated; or a heterocycle of 3 to 7 atoms wherein the heterocycle is saturated or partially unsaturated, the heterocycle containing a heteroatom selected from -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, and -N(R<sup>4</sup>)-, the heterocycle optionally containing a -C(O)-; ring B being substituted with 0-2 R<sup>5</sup>;
- 20 X is selected from O or S;
- Z is selected from a bond, -NR<sup>8</sup>C(O)-, -NR<sup>8</sup>C(S)-, -NR<sup>8</sup>C(O)NH-, -NR<sup>8</sup>C(S)NH-, -NR<sup>8</sup>SO<sub>2</sub>-, -NR<sup>8</sup>SO<sub>2</sub>NH-, -C(O)NR<sup>8</sup>-, -OC(O)NR<sup>8</sup>-, -NR<sup>8</sup>C(O)O-, -(CR<sup>15</sup>R<sup>15</sup>)<sub>1</sub>-, -CR<sup>14</sup>=CR<sup>14</sup>-, -CR<sup>15</sup>R<sup>15</sup>C(O)-, -C(O)CR<sup>15</sup>R<sup>15</sup>-, CR<sup>15</sup>R<sup>15</sup>C(=N-OR<sup>16</sup>)-, -O-CR<sup>14</sup>R<sup>14</sup>-, -CR<sup>14</sup>R<sup>14</sup>-O-, -O-, -NR<sup>9</sup>-, -NR<sup>9</sup>-CR<sup>14</sup>R<sup>14</sup>-, -CR<sup>14</sup>R<sup>14</sup>-NR<sup>9</sup>-, -S(O)<sub>p</sub>-, -S(O)<sub>p</sub>-CR<sup>14</sup>R<sup>14</sup>-, -CR<sup>14</sup>R<sup>14</sup>-S(O)<sub>p</sub>-, and -S(O)<sub>p</sub>-NR<sup>9</sup>-;
- 30 wherein neither Z nor R<sup>13</sup> are connected to a carbon atom labeled (b);

bond (a) is a single or double bond;

alternatively, when n is equal to 2, two atoms labeled  
5 (b) may join through a double bond;

E is selected from  $-S(O)_pCHRe-$ ,  $-CHReNRe-$ ,  $-C(O)-NRe-$ ,  
 $-NReC(O)NRe-$ ,  $-SO_2-NRe-$ , and  $-NReSO_2NRe-$ ;

10  $Re$  is independently selected from H and  $C_{1-3}$  alkyl;

$R^1$  is selected from a  $C_{6-10}$  aryl group substituted with  
0-5  $R^6$  and a 5-10 membered heteroaryl system  
containing 1-4 heteroatoms selected from N, O, and  
15 S, substituted with 0-3  $R^6$ ;

$R^2$  is selected from a  $C_{6-10}$  aryl group substituted with  
0-5  $R^7$  and a 5-10 membered heteroaryl system  
containing 1-4 heteroatoms selected from N, O, and  
20 S, substituted with 0-3  $R^7$ ;

$R^4$  is selected from H,  $C_{1-6}$  alkyl,  $C_{3-8}$  alkenyl,  $C_{3-8}$   
alkynyl,  $(CRR)_tOH$ ,  $(CRR)_tSH$ ,  $(CRR)_tOR^{4d}$ ,  $(CHR)_tSR^{4d}$ ,  
 $(CRR)_tNR^{4a}R^{4a}$ ,  $(CRR)_qC(O)OH$ ,  $(CRR)_rC(O)R^{4b}$ ,  
25  $(CRR)_rC(O)NR^{4a}R^{4a}$ ,  $(CRR)_tOC(O)NR^{4a}R^{4a}$ ,  
 $(CRR)_tNR^{4a}C(O)OR^{4d}$ ,  $(CRR)_tNR^{4a}C(O)R^{4b}$ ,  $(CRR)_rC(O)OR^{4d}$ ,  
 $(CRR)_tOC(O)R^{4b}$ ,  $(CRR)_rS(O)_pR^{4b}$ ,  $(CRR)_rS(O)_2NR^{4a}R^{4a}$ ,  
 $(CRR)_tNR^{4a}S(O)_2R^{4b}$ ,  $C_{1-6}$  haloalkyl, a  $(CRR)_r-C_{3-10}$   
carbocyclic residue substituted with 0-3  $R^{4e}$ , and a  
30  $(CHR)_r-4-10$  membered heterocyclic system containing  
1-4 heteroatoms selected from N, O, and S,  
substituted with 0-2  $R^{4e}$ ;

- $R^{4a}$ , at each occurrence, is independently selected from H, methyl substituted with 0-1  $R^{4c}$ ,  $C_{2-6}$  alkyl substituted with 0-3  $R^{4e}$ ,  $C_{3-8}$  alkenyl substituted with 0-3  $R^{4e}$ ,  $C_{3-8}$  alkynyl substituted with 0-3  $R^{4e}$ ,  
 5 a  $(CH_2)_r$ - $C_{3-10}$  carbocyclic residue substituted with 0-4  $R^{4e}$ , and a  $(CHR)_r$ -4-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2  $R^{4e}$ ;
- 10  $R^{4b}$ , at each occurrence, is selected from H,  $C_{1-6}$  alkyl substituted with 0-3  $R^{4e}$ ,  $C_{3-8}$  alkenyl substituted with 0-3  $R^{4e}$ ,  $C_{3-8}$  alkynyl substituted with 0-3  $R^{4e}$ , a  $(CH_2)_r$ - $C_{3-6}$  carbocyclic residue substituted with 0-2  $R^{4e}$ , and a  $(CHR)_r$ -4-10 membered heterocyclic  
 15 system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2  $R^{4e}$ ;
- $R^{4c}$  is independently selected from  $-C(O)R^{4b}$ ,  $-C(O)OR^{4d}$ ,  $-C(O)NR^{4f}R^{4f}$ , and  $(CH_2)_r$ phenyl;
- 20  $R^{4d}$ , at each occurrence, is selected from methyl,  $CF_3$ ,  $C_{2-6}$  alkyl substituted with 0-3  $R^{4e}$ ,  $C_{3-8}$  alkenyl substituted with 0-3  $R^{4e}$ ,  $C_{3-8}$  alkynyl substituted with 0-3  $R^{4e}$ , and a  $C_{3-10}$  carbocyclic residue  
 25 substituted with 0-3  $R^{4e}$ ;
- $R^{4e}$ , at each occurrence, is selected from  $C_{1-6}$  alkyl,  $C_{2-8}$  alkenyl,  $C_{2-8}$  alkynyl,  $(CH_2)_r$  $C_{3-6}$  cycloalkyl, Cl, F, Br, I, CN,  $NO_2$ ,  $(CF_2)_r$  $CF_3$ ,  $(CH_2)_r$  $OC_{1-5}$  alkyl, OH, SH,  
 30  $(CH_2)_r$  $SC_{1-5}$  alkyl,  $(CH_2)_r$  $NR^{4f}R^{4f}$ ,  $-C(O)R^{4i}$ ,  $-C(O)OR^{4j}$ ,  $-C(O)NR^{4h}R^{4h}$ ,  $-OC(O)NR^{4h}R^{4h}$ ,  $-NR^{4h}C(O)NR^{4h}R^{4h}$ ,  $-NR^{4h}C(O)OR^{4j}$ , and  $(CH_2)_r$ phenyl;

R<sup>4f</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl, C<sub>3-6</sub> cycloalkyl, and phenyl;

5 R<sup>4h</sup>, at each occurrence, is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, and a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub> carbocyclic;

10 R<sup>4i</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, and a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue;

15 R<sup>4j</sup>, at each occurrence, is selected from CF<sub>3</sub>, C<sub>1-6</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, and a C<sub>3-10</sub> carbocyclic residue;

20 R<sup>5</sup>, at each occurrence, is independently selected from H, =O, C<sub>1-6</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CRR)<sub>r</sub>OH, (CRR)<sub>r</sub>SH, (CRR)<sub>r</sub>OR<sup>5d</sup>, (CRR)<sub>r</sub>SR<sup>5d</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>R<sup>5a</sup>, (CRR)<sub>r</sub>N(→O)R<sup>5a</sup>R<sup>5a</sup>, N<sub>3</sub>, (CRR)<sub>r</sub>C(O)OH, (CRR)<sub>r</sub>C(O)R<sup>5b</sup>, (CRR)<sub>r</sub>C(O)NR<sup>5a</sup>R<sup>5a</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>C(O)R<sup>5b</sup>, (CRR)<sub>r</sub>OC(O)NR<sup>5a</sup>R<sup>5a</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>C(O)OR<sup>5d</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>C(O)NR<sup>5a</sup>R<sup>5a</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>C(O)H, (CRR)<sub>r</sub>C(O)OR<sup>5d</sup>, (CRR)<sub>r</sub>OC(O)R<sup>5b</sup>, (CRR)<sub>r</sub>S(O)<sub>p</sub>R<sup>5b</sup>, (CRR)<sub>r</sub>S(O)<sub>2</sub>NR<sup>5a</sup>R<sup>5a</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>S(O)<sub>2</sub>R<sup>5b</sup>, 25 (CRR)<sub>r</sub>NR<sup>5a</sup>S(O)<sub>2</sub>NR<sup>5a</sup>R<sup>5a</sup>, C<sub>1-6</sub> haloalkyl, a (CRR)<sub>r</sub>-C<sub>3-10</sub> carbocyclic residue substituted with 0-3 R<sup>5c</sup>, and a (CRR)<sub>r</sub>-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R<sup>5c</sup>;

30 R<sup>5a</sup>, at each occurrence, is independently selected from H, methyl substituted with 0-1 R<sup>5g</sup>, C<sub>2-6</sub> alkyl substituted with 0-2 R<sup>5e</sup>, C<sub>3-8</sub> alkenyl substituted with 0-2 R<sup>5e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>5e</sup>,

a  $(\text{CH}_2)_r\text{-C}_{3-10}$  carbocyclic residue substituted with 0-5  $\text{R}^{5e}$ , and a  $(\text{CH}_2)_r\text{-5-10}$  membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3  $\text{R}^{5e}$ ;

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$\text{R}^{5b}$ , at each occurrence, is selected from  $\text{C}_{1-6}$  alkyl substituted with 0-3  $\text{R}^{5e}$ ,  $\text{C}_{3-8}$  alkenyl substituted with 0-2  $\text{R}^{5e}$ ,  $\text{C}_{3-8}$  alkynyl substituted with 0-2  $\text{R}^{5e}$ , a  $(\text{CH}_2)_r\text{-C}_{3-6}$  carbocyclic residue substituted with 0-2  $\text{R}^{5e}$ , and a  $(\text{CH}_2)_r\text{-5-6}$  membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3  $\text{R}^{5e}$ ;

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$\text{R}^{5c}$ , at each occurrence, is selected from  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-8}$  alkenyl,  $\text{C}_{2-8}$  alkynyl,  $(\text{CH}_2)_r\text{C}_{3-6}$  cycloalkyl, Cl, Br, I, F,  $(\text{CF}_2)_r\text{CF}_3$ ,  $\text{NO}_2$ , CN,  $(\text{CH}_2)_r\text{NR}^{5f}\text{R}^{5f}$ ,  $(\text{CH}_2)_r\text{OH}$ ,  $(\text{CH}_2)_r\text{OC}_{1-4}$  alkyl,  $(\text{CH}_2)_r\text{SC}_{1-4}$  alkyl,  $(\text{CH}_2)_r\text{C}(\text{O})\text{OH}$ ,  $(\text{CH}_2)_r\text{C}(\text{O})\text{R}^{5b}$ ,  $(\text{CH}_2)_r\text{C}(\text{O})\text{NR}^{5f}\text{R}^{5f}$ ,  $(\text{CH}_2)_r\text{OC}(\text{O})\text{NR}^{5f}\text{R}^{5f}$ ,  $(\text{CH}_2)_r\text{NR}^{5f}\text{C}(\text{O})\text{R}^{5b}$ ,  $(\text{CH}_2)_r\text{C}(\text{O})\text{OC}_{1-4}$  alkyl,  $(\text{CH}_2)_r\text{NR}^{5f}\text{C}(\text{O})\text{OC}_{1-4}$  alkyl,  $(\text{CH}_2)_r\text{OC}(\text{O})\text{R}^{5b}$ ,  $(\text{CH}_2)_r\text{C}(=\text{NR}^{5f})\text{NR}^{5f}\text{R}^{5f}$ ,  $(\text{CH}_2)_r\text{S}(\text{O})_p\text{R}^{5b}$ ,  $(\text{CH}_2)_r\text{NHC}(=\text{NR}^{5f})\text{NR}^{5f}\text{R}^{5f}$ ,  $(\text{CH}_2)_r\text{S}(\text{O})_2\text{NR}^{5f}\text{R}^{5f}$ ,  $(\text{CH}_2)_r\text{NR}^{5f}\text{S}(\text{O})_2\text{R}^{5b}$ , and  $(\text{CH}_2)_r\text{phenyl}$  substituted with 0-3  $\text{R}^{5e}$ ;

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$\text{R}^{5d}$ , at each occurrence, is selected from methyl,  $\text{CF}_3$ ,  $\text{C}_{2-6}$  alkyl substituted with 0-2  $\text{R}^{5e}$ ,  $\text{C}_{3-8}$  alkenyl substituted with 0-2  $\text{R}^{5e}$ ,  $\text{C}_{3-8}$  alkynyl substituted with 0-2  $\text{R}^{5e}$ , and a  $\text{C}_{3-10}$  carbocyclic residue substituted with 0-3  $\text{R}^{5e}$ ;

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$\text{R}^{5e}$ , at each occurrence, is selected from  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-8}$  alkenyl,  $\text{C}_{2-8}$  alkynyl,  $\text{C}_{3-6}$  cycloalkyl, Cl, F, Br, I,

CN, NO<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>OC<sub>1-5</sub> alkyl, OH, SH,  
(CH<sub>2</sub>)<sub>r</sub>SC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>NR<sup>5f</sup>R<sup>5f</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

5 R<sup>5f</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl,  
and C<sub>3-6</sub> cycloalkyl;

R<sup>5g</sup> is independently selected from -C(O)R<sup>5b</sup>, -C(O)OR<sup>5d</sup>,  
-C(O)NR<sup>5f</sup>R<sup>5f</sup>, -CN, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

10 R, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl  
substituted with R<sup>5e</sup>, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl,  
(CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, and (CH<sub>2</sub>)<sub>r</sub>phenyl substituted  
with R<sup>5e</sup>;

15 R<sup>6</sup>, at each occurrence, is selected from C<sub>1-8</sub> alkyl, C<sub>2-8</sub>  
alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, Cl, Br,  
I, F, NO<sub>2</sub>, CN, (CR'R')<sub>r</sub>NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>OH,  
(CR'R')<sub>r</sub>O(CR'R')<sub>r</sub>R<sup>6d</sup>, (CR'R')<sub>r</sub>SH, (CR'R')<sub>r</sub>C(O)H,  
(CR'R')<sub>r</sub>S(CR'R')<sub>r</sub>R<sup>6d</sup>, (CR'R')<sub>r</sub>SC(O)(CR'R')<sub>r</sub>R<sup>6b</sup>,  
20 (CR'R')<sub>r</sub>C(O)OH, (CR'R')<sub>r</sub>C(O)(CR'R')<sub>r</sub>R<sup>6b</sup>,  
(CR'R')<sub>r</sub>NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>C(O)NR<sup>6a</sup>R<sup>6a</sup>,  
(CR'R')<sub>r</sub>NR<sup>6f</sup>C(O)(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>C(O)O(CR'R')<sub>r</sub>R<sup>6d</sup>,  
(CR'R')<sub>r</sub>OC(O)(CR'R')<sub>r</sub>R<sup>6b</sup>,  
(CR'R')<sub>r</sub>OC(O)NR<sup>6a</sup>(CR'R')<sub>r</sub>R<sup>6d</sup>,  
25 (CR'R')<sub>r</sub>NR<sup>6a</sup>C(O)NR<sup>6a</sup>(CR'R')<sub>r</sub>R<sup>6d</sup>,  
(CR'R')<sub>r</sub>NR<sup>6a</sup>C(S)NR<sup>6a</sup>(CR'R')<sub>r</sub>R<sup>6d</sup>,  
(CR'R')<sub>r</sub>NR<sup>6f</sup>C(O)O(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>C(=NR<sup>6f</sup>)NR<sup>6a</sup>R<sup>6a</sup>,  
(CR'R')<sub>r</sub>NHC(=NR<sup>6f</sup>)NR<sup>6f</sup>R<sup>6f</sup>, (CR'R')<sub>r</sub>S(O)<sub>p</sub>(CR'R')<sub>r</sub>R<sup>6b</sup>,  
(CR'R')<sub>r</sub>S(O)<sub>2</sub>NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>NR<sup>6f</sup>S(O)<sub>2</sub>NR<sup>6a</sup>R<sup>6a</sup>,  
30 (CR'R')<sub>r</sub>NR<sup>6f</sup>S(O)<sub>2</sub>(CR'R')<sub>r</sub>R<sup>6b</sup>, C<sub>1-6</sub> haloalkyl, C<sub>2-8</sub>  
alkenyl substituted with 0-3 R', C<sub>2-8</sub> alkynyl  
substituted with 0-3 R', (CR'R')<sub>r</sub>phenyl substituted  
with 0-3 R<sup>6e</sup>, and a (CH<sub>2</sub>)<sub>r-5-6</sub> membered heterocyclic

system containing 1-2 heteroatoms selected from N, O, and S, substituted with 0-2 R<sup>6e</sup>;

alternatively, two R<sup>6</sup> on adjacent atoms on R<sup>1</sup> may join to  
5 form a cyclic acetal;

R<sup>6a</sup>, at each occurrence, is selected from H, methyl substituted with 0-1 R<sup>6g</sup>, C<sub>2-6</sub> alkyl substituted with 0-2 R<sup>6e</sup>, C<sub>3-8</sub> alkenyl substituted with 0-2 R<sup>6e</sup>, C<sub>3-8</sub>  
10 alkynyl substituted with 0-2 R<sup>6e</sup>, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub> carbocyclic residue substituted with 0-5 R<sup>6e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R<sup>6e</sup>;

15 R<sup>6b</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl substituted with 0-2 R<sup>6e</sup>, C<sub>3-8</sub> alkenyl substituted with 0-2 R<sup>6e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>6e</sup>, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue substituted with 0-3  
20 R<sup>6e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R<sup>6e</sup>;

R<sup>6d</sup>, at each occurrence, is selected from C<sub>3-8</sub> alkenyl substituted with 0-2 R<sup>6e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>6e</sup>, methyl, CF<sub>3</sub>, C<sub>2-6</sub> alkyl substituted with 0-3 R<sup>6e</sup>, C<sub>2-4</sub> haloalkyl, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub>  
25 carbocyclic residue substituted with 0-3 R<sup>6e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S,  
30 substituted with 0-3 R<sup>6e</sup>;

R<sup>6e</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> cycloalkyl, Cl, F,

Br, I, CN, NO<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>OC<sub>1-5</sub> alkyl, OH, SH,  
(CH<sub>2</sub>)<sub>r</sub>SC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>NR<sup>6f</sup>R<sup>6f</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

5 R<sup>6f</sup>, at each occurrence, is selected from H, C<sub>1-5</sub> alkyl,  
and C<sub>3-6</sub> cycloalkyl, and phenyl;

R<sup>6g</sup> is independently selected from -C(O)R<sup>6b</sup>, -C(O)OR<sup>6d</sup>,  
-C(O)NR<sup>6f</sup>R<sup>6f</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

10 R<sup>7</sup>, at each occurrence, is selected from C<sub>1-8</sub> alkyl, C<sub>2-8</sub>  
alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, Cl, Br,  
I, F, NO<sub>2</sub>, CN, (CR'R')<sub>r</sub>NR<sup>7a</sup>R<sup>7a</sup>, (CR'R')<sub>r</sub>OH,  
(CR'R')<sub>r</sub>O(CR'R')<sub>r</sub>R<sup>7d</sup>, (CR'R')<sub>r</sub>SH, (CR'R')<sub>r</sub>C(O)H,  
(CR'R')<sub>r</sub>S(CR'R')<sub>r</sub>R<sup>7d</sup>, (CR'R')<sub>r</sub>C(O)OH,  
15 (CR'R')<sub>r</sub>C(O)(CR'R')<sub>r</sub>R<sup>7b</sup>, (CR'R')<sub>r</sub>C(O)NR<sup>7a</sup>R<sup>7a</sup>,  
(CR'R')<sub>r</sub>NR<sup>7f</sup>C(O)(CR'R')<sub>r</sub>R<sup>7b</sup>, (CR'R')<sub>r</sub>C(O)O(CR'R')<sub>r</sub>R<sup>7d</sup>,  
(CR'R')<sub>r</sub>OC(O)(CR'R')<sub>r</sub>R<sup>7b</sup>,  
(CR'R')<sub>r</sub>OC(O)NR<sup>7a</sup>(CR'R')<sub>r</sub>R<sup>7a</sup>,  
(CR'R')<sub>r</sub>NR<sup>7a</sup>C(O)NR<sup>7a</sup>(CR'R')<sub>r</sub>R<sup>7a</sup>,  
20 (CR'R')<sub>r</sub>NR<sup>7f</sup>C(O)O(CR'R')<sub>r</sub>R<sup>7d</sup>, (CR'R')<sub>r</sub>C(=NR<sup>7f</sup>)NR<sup>7a</sup>R<sup>7a</sup>,  
(CR'R')<sub>r</sub>NHC(=NR<sup>7f</sup>)NR<sup>7f</sup>R<sup>7f</sup>, (CR'R')<sub>r</sub>S(O)<sub>p</sub>(CR'R')<sub>r</sub>R<sup>7b</sup>,  
(CR'R')<sub>r</sub>S(O)<sub>2</sub>NR<sup>7a</sup>R<sup>7a</sup>, (CR'R')<sub>r</sub>NR<sup>7a</sup>S(O)<sub>2</sub>NR<sup>7a</sup>R<sup>7a</sup>,  
(CR'R')<sub>r</sub>NR<sup>7f</sup>S(O)<sub>2</sub>(CR'R')<sub>r</sub>R<sup>7b</sup>, C<sub>1-6</sub> haloalkyl, C<sub>2-8</sub>  
alkenyl substituted with 0-3 R', C<sub>2-8</sub> alkynyl  
25 substituted with 0-3 R', (CR'R')<sub>r</sub> C<sub>3-10</sub> carbocyclic  
residue and (CR'R')<sub>r</sub>phenyl substituted with 0-3 R<sup>7e</sup>;

alternatively, two R<sup>7</sup> on adjacent atoms on R<sup>2</sup> may join to  
form a cyclic acetal;

30

R<sup>7a</sup>, at each occurrence, is independently selected from H,  
methyl substituted with 0-1 R<sup>7g</sup>, C<sub>2-6</sub> alkyl  
substituted with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkenyl substituted



with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>7e</sup>,  
 a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub> carbocyclic residue substituted with  
 0-5 R<sup>7e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-10 membered heterocyclic  
 system containing 1-4 heteroatoms selected from N,  
 5 O, and S, substituted with 0-2 R<sup>7e</sup>;

R<sup>7b</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl  
 substituted with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkenyl substituted  
 with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>7e</sup>,  
 10 a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue substituted with 0-3  
 R<sup>7e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic system  
 containing 1-4 heteroatoms selected from N, O, and  
 S, substituted with 0-2 R<sup>7e</sup>;

15 R<sup>7d</sup>, at each occurrence, is selected from C<sub>3-8</sub> alkenyl  
 substituted with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkynyl substituted  
 with 0-2 R<sup>7e</sup>, methyl, CF<sub>3</sub>, C<sub>2-4</sub> haloalkyl, C<sub>2-6</sub> alkyl  
 substituted with 0-3 R<sup>7e</sup>, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub> carbocyclic  
 residue substituted with 0-3 R<sup>7e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6  
 20 membered heterocyclic system containing 1-4  
 heteroatoms selected from N, O, and S, substituted  
 with 0-3 R<sup>7e</sup>;

R<sup>7e</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub>  
 25 alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> cycloalkyl, Cl, F,  
 Br, I, CN, NO<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>OC<sub>1-5</sub> alkyl, OH, SH,  
 C(O)OC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>SC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>NR<sup>7f</sup>R<sup>7f</sup>, and  
 (CH<sub>2</sub>)<sub>r</sub>phenyl;

30 R<sup>7f</sup>, at each occurrence, is selected from H, C<sub>1-5</sub> alkyl,  
 and C<sub>3-6</sub> cycloalkyl, and phenyl;

R<sup>7g</sup> is independently selected from -C(O)R<sup>7b</sup>, -C(O)OR<sup>7d</sup>,  
 -C(O)NR<sup>7f</sup>R<sup>7f</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

R', at each occurrence, is selected from H, C<sub>1-6</sub> alkyl substituted with R<sup>6e</sup>, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, and (CH<sub>2</sub>)<sub>r</sub>phenyl substituted with R<sup>6e</sup>;

R<sup>8</sup> is selected from H, C<sub>1-4</sub> alkyl, and C<sub>3-4</sub> cycloalkyl;

R<sup>9</sup> is selected from H, C<sub>1-4</sub> alkyl, C<sub>3-4</sub> cycloalkyl, -C(O)H, and -C(O)-C<sub>1-4</sub>alkyl;

R<sup>10</sup> is independently selected from H, and C<sub>1-4</sub>alkyl substituted with 0-1 R<sup>10b</sup>, alternatively, two R<sup>10</sup> form =O;

R<sup>10b</sup>, at each occurrence, is independently selected from -OH, -SH, -NR<sup>10c</sup>R<sup>10c</sup>, -C(O)NR<sup>10c</sup>R<sup>10c</sup>, and -NHC(O)R<sup>10c</sup>;

R<sup>10c</sup> is selected from H, C<sub>1-4</sub> alkyl and C<sub>3-6</sub> cycloalkyl;

R<sup>11</sup> is selected from H, C<sub>1-4</sub> alkyl, (CHR)<sub>q</sub>OH, (CHR)<sub>q</sub>SH, (CHR)<sub>q</sub>OR<sup>11d</sup>, (CHR)<sub>q</sub>S(O)<sub>p</sub>R<sup>11d</sup>, (CHR)<sub>r</sub>C(O)R<sup>11b</sup>, (CHR)<sub>r</sub>NR<sup>11a</sup>R<sup>11a</sup>, (CHR)<sub>r</sub>C(O)NR<sup>11a</sup>R<sup>11a</sup>, (CHR)<sub>r</sub>C(O)NR<sup>11a</sup>OR<sup>11d</sup>, (CHR)<sub>q</sub>NR<sup>11a</sup>C(O)R<sup>11b</sup>, (CHR)<sub>q</sub>NR<sup>11a</sup>C(O)OR<sup>11d</sup>, (CHR)<sub>q</sub>OC(O)NR<sup>11a</sup>R<sup>11a</sup>, (CHR)<sub>r</sub>C(O)OR<sup>11d</sup>, a (CHR)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue substituted with 0-5 R<sup>11e</sup>, and a (CHR)<sub>r</sub>-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R<sup>11e</sup>;

R<sup>11a</sup>, at each occurrence, is independently selected from H, C<sub>1-4</sub> alkyl, C<sub>3-4</sub> alkenyl, C<sub>3-4</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue

substituted with 0-5  $R^{11e}$ , and a  $(CH_2)_r$ -5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3  $R^{11e}$ ;

5  $R^{11b}$ , at each occurrence, is independently selected from  $C_{1-4}$  alkyl,  $C_{2-4}$  alkenyl,  $C_{2-4}$  alkynyl, a  $(CH_2)_r$ - $C_{3-6}$  carbocyclic residue substituted with 0-2  $R^{11e}$ , and a  $(CH_2)_r$ -5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S,  
 10 substituted with 0-3  $R^{11e}$ ;

$R^{11d}$ , at each occurrence, is independently selected from H, methyl,  $-CF_3$ ,  $C_{2-4}$  alkyl,  $C_{3-6}$  alkenyl,  $C_{3-6}$  alkynyl, a  $C_{3-6}$  carbocyclic residue substituted with  
 15 0-3  $R^{11e}$ , and a  $(CH_2)_r$ -5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3  $R^{11e}$ ;

$R^{11e}$ , at each occurrence, is selected from  $C_{1-6}$  alkyl,  $C_{2-8}$  alkenyl,  $C_{2-8}$  alkynyl,  $C_{3-6}$  cycloalkyl, Cl, F, Br, I, CN,  $NO_2$ ,  $(CF_2)_rCF_3$ ,  $(CH_2)_rOC_{1-5}$  alkyl, OH,  $-O-C_{1-6}$  alkyl, SH,  $(CH_2)_rSC_{1-5}$  alkyl,  $(CH_2)_rNR^{11f}R^{11f}$ , and  $(CH_2)_r$ phenyl;

25  $R^{11f}$ , at each occurrence, is selected from H,  $C_{1-6}$  alkyl, and  $C_{3-6}$  cycloalkyl;

$R^{12}$  is selected from H,  $C_{1-4}$  alkyl,  $(CHR)_qOH$ ,  $(CHR)_qSH$ ,  $(CHR)_qOR^{12d}$ ,  $(CHR)_qS(O)_pR^{12d}$ ,  $(CHR)_rC(O)R^{12b}$ ,  
 30  $(CHR)_rNR^{12a}R^{12a}$ ,  $(CHR)_rC(O)NR^{12a}R^{12a}$ ,  $(CHR)_rC(O)NR^{12a}OR^{12d}$ ,  $(CHR)_qNR^{12a}C(O)R^{12b}$ ,

(CHR)<sub>q</sub>NR<sup>12a</sup>C(O)OR<sup>12d</sup>, (CHR)<sub>q</sub>OC(O)NR<sup>12a</sup>R<sup>12a</sup>,  
 (CHR)<sub>r</sub>C(O)OR<sup>12d</sup>, a (CHR)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue  
 substituted with 0-5 R<sup>12e</sup>, and a (CHR)<sub>r</sub>-5-10 membered  
 heterocyclic system containing 1-4 heteroatoms  
 5 selected from N, O, and S, substituted with 0-3 R<sup>12e</sup>;

R<sup>12a</sup>, at each occurrence, is independently selected from  
 H, C<sub>1-4</sub> alkyl, C<sub>3-4</sub> alkenyl, C<sub>3-4</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub>  
 cycloalkyl, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue  
 10 substituted with 0-5 R<sup>12e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered  
 heterocyclic system containing 1-4 heteroatoms  
 selected from N, O, and S, substituted with 0-3 R<sup>12e</sup>;

R<sup>12b</sup>, at each occurrence, is independently selected from  
 15 C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub>  
 carbocyclic residue substituted with 0-2 R<sup>12e</sup>, and a  
 (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic system containing  
 1-4 heteroatoms selected from N, O, and S,  
 substituted with 0-3 R<sup>12e</sup>;

20 R<sup>12d</sup>, at each occurrence, is independently selected from  
 H, methyl, -CF<sub>3</sub>, C<sub>2-4</sub> alkyl, C<sub>3-6</sub> alkenyl, C<sub>3-6</sub>  
 alkynyl, a C<sub>3-6</sub> carbocyclic residue substituted with  
 0-3 R<sup>12e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic  
 25 system containing 1-4 heteroatoms selected from N,  
 O, and S, substituted with 0-3 R<sup>12e</sup>;

R<sup>12e</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub>  
 alkenyl, C<sub>2-8</sub> alkynyl, C<sub>3-6</sub> cycloalkyl, Cl, F, Br, I,  
 30 CN, NO<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>OC<sub>1-5</sub> alkyl, OH, -O-C<sub>1-6</sub>

alkyl, SH,  $(\text{CH}_2)_r\text{SC}_{1-5}$  alkyl,  $(\text{CH}_2)_r\text{NR}^{12f}\text{R}^{12f}$ , and  
 $(\text{CH}_2)_r\text{phenyl}$ ;

$\text{R}^{12f}$ , at each occurrence, is selected from H,  $\text{C}_{1-6}$  alkyl,  
 5 and  $\text{C}_{3-6}$  cycloalkyl;

$\text{R}^{13}$ , at each occurrence, is independently selected from H,  
 and  $\text{C}_{1-4}$ alkyl substituted with 0-1  $\text{R}^{13b}$ , -OH,  $-\text{NH}_2$ ,  
 F, Cl, Br, I,  $-\text{OR}^{13a}$ ,  $-\text{N}(\text{R}^{13a})_2$ , and  $\text{C}_{1-4}$  alkyl  
 10 substituted with 0-3  $\text{R}^{13b}$ ;

$\text{R}^{13a}$  is selected from H,  $\text{C}_{1-4}$  alkyl and  $\text{C}_{3-6}$  cycloalkyl;

$\text{R}^{13b}$ , at each occurrence, is independently selected from  
 15 -OH, -SH,  $-\text{NR}^{13c}\text{R}^{13c}$ ,  $-\text{C}(\text{O})\text{NR}^{13c}\text{R}^{13c}$ , and  $-\text{NHC}(\text{O})\text{R}^{13c}$ ;

$\text{R}^{13c}$  is selected from H,  $\text{C}_{1-4}$  alkyl and  $\text{C}_{3-6}$  cycloalkyl;

$\text{R}^{14}$ , at each occurrence, is independently selected from H  
 20 and  $\text{C}_{1-4}$ alkyl;

alternatively, two  $\text{R}^{14}$ s, along with the carbon atom to  
 which they are attached, join to form a  $\text{C}_{3-6}$   
 carbocyclic ring;

25  $\text{R}^{15}$ , at each occurrence, is independently selected from H,  
 $\text{C}_{1-4}$ alkyl, OH,  $\text{NH}_2$ ,  $-\text{O}-\text{C}_{1-4}$  alkyl,  $\text{NR}^{15a}\text{R}^{15a}$ ,  
 $\text{C}(\text{O})\text{NR}^{15a}\text{R}^{15a}$ ,  $\text{NR}^{15a}\text{C}(\text{O})\text{R}^{15b}$ ,  $\text{NR}^{15a}\text{C}(\text{O})\text{OR}^{15d}$ ,  
 $\text{OC}(\text{O})\text{NR}^{15a}\text{R}^{15a}$ , and  $(\text{CHR})_r\text{C}(\text{O})\text{OR}^{15d}$ ;

30

alternatively, two R<sup>15</sup>s, along with the carbon atom or atoms to which they are attached, join to form a C<sub>3-6</sub> carbocyclic ring;

5 R<sup>15a</sup>, at each occurrence, is independently selected from H, and C<sub>1-4</sub> alkyl;

R<sup>15b</sup>, at each occurrence, is independently selected from C<sub>1-4</sub> alkyl, C<sub>3-6</sub> alkenyl, and C<sub>3-6</sub> alkynyl;

10

R<sup>15d</sup>, at each occurrence, is independently selected from C<sub>1-4</sub> alkyl, C<sub>3-6</sub> alkenyl, and C<sub>3-6</sub> alkynyl;

R<sup>16</sup> is selected from C<sub>1-4</sub> alkyl;

15

l is selected from 1, 2 and 3;

n is selected from 0, 1, 2, and 3;

20 m is selected from 0 and 1;

p, at each occurrence, is independently selected from 0, 1, and 2;

25 q, at each occurrence, is independently selected from 1, 2, 3, and 4;

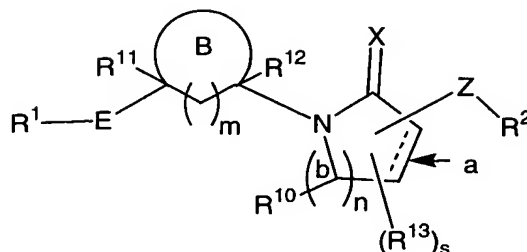
r, at each occurrence, is independently selected from 0, 1, 2, 3, and 4;

30

t, at each occurrence, is independently selected from 2, 3, and 4;

s is selected from 0 and 1.

2. A compound of claim 1, wherein the compound is of formula (I):



(I)

or a stereoisomer or a pharmaceutically acceptable salt thereof, wherein:

10 ring B is a cycloalkyl group of 3 to 8 carbon atoms wherein the cycloalkyl group is saturated or partially unsaturated; or a heterocycle of 3 to 7 atoms wherein the heterocycle is saturated or partially unsaturated, the heterocycle containing a  
15 heteroatom selected from -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, and -N(R<sup>4</sup>)-, the heterocycle optionally containing a -C(O)-; ring B being substituted with 0-2 R<sup>5</sup>;

20 X is selected from O or S;

Z is selected from a bond, -NR<sup>8</sup>C(O)-, -NR<sup>8</sup>C(S)-, -NR<sup>8</sup>C(O)NH-, -NR<sup>8</sup>C(S)NH-, -NR<sup>8</sup>SO<sub>2</sub>-, -NR<sup>8</sup>SO<sub>2</sub>NH-, -C(O)NR<sup>8</sup>-, -OC(O)NR<sup>8</sup>-, -NR<sup>8</sup>C(O)O-, -(CR<sup>15</sup>R<sup>15</sup>)<sub>1</sub>-,  
25 -CR<sup>14</sup>=CR<sup>14</sup>-, -CR<sup>15</sup>R<sup>15</sup>C(O)-, -C(O)CR<sup>15</sup>R<sup>15</sup>-, CR<sup>15</sup>R<sup>15</sup>C(=N-OR<sup>16</sup>)-, -O-CR<sup>14</sup>R<sup>14</sup>-, -CR<sup>14</sup>R<sup>14</sup>-O-, -O-, -NR<sup>9</sup>-, -NR<sup>9</sup>-CR<sup>14</sup>R<sup>14</sup>-, -CR<sup>14</sup>R<sup>14</sup>-NR<sup>9</sup>-, -S(O)<sub>p</sub>-, -S(O)<sub>p</sub>-CR<sup>14</sup>R<sup>14</sup>-, -CR<sup>14</sup>R<sup>14</sup>-S(O)<sub>p</sub>-, and -S(O)<sub>p</sub>-NR<sup>9</sup>-;

30 wherein neither Z nor R<sup>13</sup> are connected to a carbon atom labeled (b);

bond (a) is a single or double bond;

alternatively, when n is equal to 2, two atoms labeled  
5 (b) may join through a double bond;

E is selected from  $-S(O)_pCHRe-$ ,  $-CHReNRe-$ ,  $-C(O)-NRe-$ ,  
 $-NReC(O)NRe-$ ,  $-SO_2-NRe-$ , and  $-NReSO_2NRe-$ ;

10  $Re$  is independently selected from H and  $C_{1-3}$  alkyl;

$R^1$  is selected from a  $C_{6-10}$  aryl group substituted with  
0-5  $R^6$  and a 5-10 membered heteroaryl system  
containing 1-4 heteroatoms selected from N, O, and  
15 S, substituted with 0-3  $R^6$ ;

$R^2$  is selected from a  $C_{6-10}$  aryl group substituted with  
0-5  $R^7$  and a 5-10 membered heteroaryl system  
containing 1-4 heteroatoms selected from N, O, and  
20 S, substituted with 0-3  $R^7$ ;

$R^4$  is selected from H,  $C_{1-6}$  alkyl,  $C_{3-8}$  alkenyl,  $C_{3-8}$   
alkynyl,  $(CRR)_tOH$ ,  $(CRR)_tSH$ ,  $(CRR)_tOR^{4d}$ ,  $(CHR)_tSR^{4d}$ ,  
 $(CRR)_tNR^{4a}R^{4a}$ ,  $(CRR)_qC(O)OH$ ,  $(CRR)_rC(O)R^{4b}$ ,  
25  $(CRR)_rC(O)NR^{4a}R^{4a}$ ,  $(CRR)_tOC(O)NR^{4a}R^{4a}$ ,  
 $(CRR)_tNR^{4a}C(O)OR^{4d}$ ,  $(CRR)_tNR^{4a}C(O)R^{4b}$ ,  $(CRR)_rC(O)OR^{4d}$ ,  
 $(CRR)_tOC(O)R^{4b}$ ,  $(CRR)_rS(O)_pR^{4b}$ ,  $(CRR)_rS(O)_2NR^{4a}R^{4a}$ ,  
 $(CRR)_tNR^{4a}S(O)_2R^{4b}$ ,  $C_{1-6}$  haloalkyl, a  $(CRR)_r-C_{3-10}$   
carbocyclic residue substituted with 0-3  $R^{4e}$ , and a  
30  $(CHR)_r-4-10$  membered heterocyclic system containing  
1-4 heteroatoms selected from N, O, and S,  
substituted with 0-2  $R^{4e}$ ;



$R^{4a}$ , at each occurrence, is independently selected from H,  
 methyl substituted with 0-1  $R^{4c}$ ,  $C_{2-6}$  alkyl  
 substituted with 0-3  $R^{4e}$ ,  $C_{3-8}$  alkenyl substituted  
 with 0-3  $R^{4e}$ ,  $C_{3-8}$  alkynyl substituted with 0-3  $R^{4e}$ ,  
 5 a  $(CH_2)_r$ - $C_{3-10}$  carbocyclic residue substituted with  
 0-4  $R^{4e}$ , and a  $(CHR)_r$ -4-10 membered heterocyclic  
 system containing 1-4 heteroatoms selected from N,  
 O, and S, substituted with 0-2  $R^{4e}$ ;

10  $R^{4b}$ , at each occurrence, is selected from H,  $C_{1-6}$  alkyl  
 substituted with 0-3  $R^{4e}$ ,  $C_{3-8}$  alkenyl substituted  
 with 0-3  $R^{4e}$ ,  $C_{3-8}$  alkynyl substituted with 0-3  $R^{4e}$ ,  
 a  $(CH_2)_r$ - $C_{3-6}$  carbocyclic residue substituted with  
 0-2  $R^{4e}$ , and a  $(CHR)_r$ -4-10 membered heterocyclic  
 15 system containing 1-4 heteroatoms selected from N,  
 O, and S, substituted with 0-2  $R^{4e}$ ;

$R^{4c}$  is independently selected from  $-C(O)R^{4b}$ ,  $-C(O)OR^{4d}$ ,  
 $-C(O)NR^{4f}R^{4f}$ , and  $(CH_2)_r$ phenyl;

20  $R^{4d}$ , at each occurrence, is selected from methyl,  $CF_3$ ,  
 $C_{2-6}$  alkyl substituted with 0-3  $R^{4e}$ ,  $C_{3-8}$  alkenyl  
 substituted with 0-3  $R^{4e}$ ,  $C_{3-8}$  alkynyl substituted  
 with 0-3  $R^{4e}$ , and a  $C_{3-10}$  carbocyclic residue  
 25 substituted with 0-3  $R^{4e}$ ;

$R^{4e}$ , at each occurrence, is selected from  $C_{1-6}$  alkyl,  $C_{2-8}$   
 alkenyl,  $C_{2-8}$  alkynyl,  $(CH_2)_r$  $C_{3-6}$  cycloalkyl, Cl, F,  
 Br, I, CN,  $NO_2$ ,  $(CF_2)_r$  $CF_3$ ,  $(CH_2)_r$  $OC_{1-5}$  alkyl, OH, SH,  
 30  $(CH_2)_r$  $SC_{1-5}$  alkyl,  $(CH_2)_r$  $NR^{4f}R^{4f}$ ,  $-C(O)R^{4i}$ ,  $-C(O)OR^{4j}$ ,  
 $-C(O)NR^{4h}R^{4h}$ ,  $-OC(O)NR^{4h}R^{4h}$ ,  $-NR^{4h}C(O)NR^{4h}R^{4h}$ ,  
 $-NR^{4h}C(O)OR^{4j}$ , and  $(CH_2)_r$ phenyl;

- R<sup>4f</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl, C<sub>3-6</sub> cycloalkyl, and phenyl;
- 5 R<sup>4h</sup>, at each occurrence, is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, and a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub> carbocyclic;
- 10 R<sup>4i</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, and a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue;
- 15 R<sup>4j</sup>, at each occurrence, is selected from CF<sub>3</sub>, C<sub>1-6</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, and a C<sub>3-10</sub> carbocyclic residue;
- 20 R<sup>5</sup>, at each occurrence, is independently selected from H, =O, C<sub>1-6</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CRR)<sub>r</sub>OH, (CRR)<sub>r</sub>SH, (CRR)<sub>r</sub>OR<sup>5d</sup>, (CRR)<sub>r</sub>SR<sup>5d</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>R<sup>5a</sup>, (CRR)<sub>r</sub>C(O)OH, (CRR)<sub>r</sub>C(O)R<sup>5b</sup>, (CRR)<sub>r</sub>C(O)NR<sup>5a</sup>R<sup>5a</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>C(O)R<sup>5b</sup>, (CRR)<sub>r</sub>OC(O)NR<sup>5a</sup>R<sup>5a</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>C(O)OR<sup>5d</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>C(O)NR<sup>5a</sup>R<sup>5a</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>C(O)H, (CRR)<sub>r</sub>C(O)OR<sup>5d</sup>, (CRR)<sub>r</sub>OC(O)R<sup>5b</sup>, (CRR)<sub>r</sub>S(O)<sub>p</sub>R<sup>5b</sup>, (CRR)<sub>r</sub>S(O)<sub>2</sub>NR<sup>5a</sup>R<sup>5a</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>S(O)<sub>2</sub>R<sup>5b</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>S(O)<sub>2</sub>NR<sup>5a</sup>R<sup>5a</sup>, C<sub>1-6</sub> haloalkyl, a (CRR)<sub>r</sub>-C<sub>3-10</sub> carbocyclic residue substituted with 0-3 R<sup>5c</sup>, and a (CRR)<sub>r</sub>-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R<sup>5c</sup>;
- 25
- 30 R<sup>5a</sup>, at each occurrence, is independently selected from H, methyl substituted with 0-1 R<sup>5g</sup>, C<sub>2-6</sub> alkyl substituted with 0-2 R<sup>5e</sup>, C<sub>3-8</sub> alkenyl substituted with 0-2 R<sup>5e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>5e</sup>, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub> carbocyclic residue substituted with

0-5 R<sup>5e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R<sup>5e</sup>;

5 R<sup>5b</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl substituted with 0-3 R<sup>5e</sup>, C<sub>3-8</sub> alkenyl substituted with 0-2 R<sup>5e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>5e</sup>, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue substituted with 0-2 R<sup>5e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic  
10 system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R<sup>5e</sup>;

R<sup>5c</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> cycloalkyl, Cl, Br,  
15 I, F, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, NO<sub>2</sub>, CN, (CH<sub>2</sub>)<sub>r</sub>NR<sup>5f</sup>R<sup>5f</sup>, (CH<sub>2</sub>)<sub>r</sub>OH, (CH<sub>2</sub>)<sub>r</sub>OC<sub>1-4</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>SC<sub>1-4</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>C(O)OH, (CH<sub>2</sub>)<sub>r</sub>C(O)R<sup>5b</sup>, (CH<sub>2</sub>)<sub>r</sub>C(O)NR<sup>5f</sup>R<sup>5f</sup>, (CH<sub>2</sub>)<sub>r</sub>OC(O)NR<sup>5f</sup>R<sup>5f</sup>, (CH<sub>2</sub>)<sub>r</sub>NR<sup>5f</sup>C(O)R<sup>5b</sup>, (CH<sub>2</sub>)<sub>r</sub>C(O)OC<sub>1-4</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>NR<sup>5f</sup>C(O)OC<sub>1-4</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>OC(O)R<sup>5b</sup>,  
20 (CH<sub>2</sub>)<sub>r</sub>C(=NR<sup>5f</sup>)NR<sup>5f</sup>R<sup>5f</sup>, (CH<sub>2</sub>)<sub>r</sub>S(O)<sub>p</sub>R<sup>5b</sup>, (CH<sub>2</sub>)<sub>r</sub>NHC(=NR<sup>5f</sup>)NR<sup>5f</sup>R<sup>5f</sup>, (CH<sub>2</sub>)<sub>r</sub>S(O)<sub>2</sub>NR<sup>5f</sup>R<sup>5f</sup>, (CH<sub>2</sub>)<sub>r</sub>NR<sup>5f</sup>S(O)<sub>2</sub>R<sup>5b</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl substituted with 0-3 R<sup>5e</sup>;

25 R<sup>5d</sup>, at each occurrence, is selected from methyl, CF<sub>3</sub>, C<sub>2-6</sub> alkyl substituted with 0-2 R<sup>5e</sup>, C<sub>3-8</sub> alkenyl substituted with 0-2 R<sup>5e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>5e</sup>, and a C<sub>3-10</sub> carbocyclic residue substituted with 0-3 R<sup>5e</sup>;

30 R<sup>5e</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, C<sub>3-6</sub> cycloalkyl, Cl, F, Br, I,

CN, NO<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>OC<sub>1-5</sub> alkyl, OH, SH,  
(CH<sub>2</sub>)<sub>r</sub>SC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>NR<sup>5f</sup>R<sup>5f</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

5 R<sup>5f</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl,  
and C<sub>3-6</sub> cycloalkyl;

R<sup>5g</sup> is independently selected from -C(O)R<sup>5b</sup>, -C(O)OR<sup>5d</sup>,  
-C(O)NR<sup>5f</sup>R<sup>5f</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

10 R, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl  
substituted with R<sup>5e</sup>, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl,  
(CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, and (CH<sub>2</sub>)<sub>r</sub>phenyl substituted  
with R<sup>5e</sup>;

15 R<sup>6</sup>, at each occurrence, is selected from C<sub>1-8</sub> alkyl, C<sub>2-8</sub>  
alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, Cl, Br,  
I, F, NO<sub>2</sub>, CN, (CR'R')<sub>r</sub>NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>OH,  
(CR'R')<sub>r</sub>O(CR'R')<sub>r</sub>R<sup>6d</sup>, (CR'R')<sub>r</sub>SH, (CR'R')<sub>r</sub>C(O)H,  
(CR'R')<sub>r</sub>S(CR'R')<sub>r</sub>R<sup>6d</sup>, (CR'R')<sub>r</sub>SC(O)(CR'R')<sub>r</sub>R<sup>6b</sup>,  
20 (CR'R')<sub>r</sub>C(O)OH, (CR'R')<sub>r</sub>C(O)(CR'R')<sub>r</sub>R<sup>6b</sup>,  
(CR'R')<sub>r</sub>NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>C(O)NR<sup>6a</sup>R<sup>6a</sup>,  
(CR'R')<sub>r</sub>NR<sup>6f</sup>C(O)(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>C(O)O(CR'R')<sub>r</sub>R<sup>6d</sup>,  
(CR'R')<sub>r</sub>OC(O)(CR'R')<sub>r</sub>R<sup>6b</sup>,  
(CR'R')<sub>r</sub>OC(O)NR<sup>6a</sup>(CR'R')<sub>r</sub>R<sup>6d</sup>,  
25 (CR'R')<sub>r</sub>NR<sup>6a</sup>C(O)NR<sup>6a</sup>(CR'R')<sub>r</sub>R<sup>6d</sup>,  
(CR'R')<sub>r</sub>NR<sup>6a</sup>C(S)NR<sup>6a</sup>(CR'R')<sub>r</sub>R<sup>6d</sup>,  
(CR'R')<sub>r</sub>NR<sup>6f</sup>C(O)O(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>C(=NR<sup>6f</sup>)NR<sup>6a</sup>R<sup>6a</sup>,  
(CR'R')<sub>r</sub>NHC(=NR<sup>6f</sup>)NR<sup>6f</sup>R<sup>6f</sup>, (CR'R')<sub>r</sub>S(O)<sub>p</sub>(CR'R')<sub>r</sub>R<sup>6b</sup>,  
(CR'R')<sub>r</sub>S(O)<sub>2</sub>NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>NR<sup>6f</sup>S(O)<sub>2</sub>NR<sup>6a</sup>R<sup>6a</sup>,  
30 (CR'R')<sub>r</sub>NR<sup>6f</sup>S(O)<sub>2</sub>(CR'R')<sub>r</sub>R<sup>6b</sup>, C<sub>1-6</sub> haloalkyl, C<sub>2-8</sub>  
alkenyl substituted with 0-3 R', C<sub>2-8</sub> alkynyl  
substituted with 0-3 R', (CR'R')<sub>r</sub>phenyl substituted  
with 0-3 R<sup>6e</sup>, and a (CH<sub>2</sub>)<sub>r-5-6</sub> membered heterocyclic

system containing 1-2 heteroatoms selected from N, O, and S, substituted with 0-2 R<sup>6e</sup>;

alternatively, two R<sup>6</sup> on adjacent atoms on R<sup>1</sup> may join to  
5 form a cyclic acetal;

R<sup>6a</sup>, at each occurrence, is selected from H, methyl substituted with 0-1 R<sup>6g</sup>, C<sub>2-6</sub> alkyl substituted with 0-2 R<sup>6e</sup>, C<sub>3-8</sub> alkenyl substituted with 0-2 R<sup>6e</sup>, C<sub>3-8</sub>  
10 alkynyl substituted with 0-2 R<sup>6e</sup>, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub> carbocyclic residue substituted with 0-5 R<sup>6e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R<sup>6e</sup>;

15 R<sup>6b</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl substituted with 0-2 R<sup>6e</sup>, C<sub>3-8</sub> alkenyl substituted with 0-2 R<sup>6e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>6e</sup>, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue substituted with 0-3  
20 R<sup>6e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R<sup>6e</sup>;

R<sup>6d</sup>, at each occurrence, is selected from C<sub>3-8</sub> alkenyl substituted with 0-2 R<sup>6e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>6e</sup>, methyl, CF<sub>3</sub>, C<sub>2-6</sub> alkyl substituted with 0-3 R<sup>6e</sup>, C<sub>2-4</sub> haloalkyl, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub>  
25 carbocyclic residue substituted with 0-3 R<sup>6e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S,  
30 substituted with 0-3 R<sup>6e</sup>;

R<sup>6e</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> cycloalkyl, Cl, F,

Br, I, CN, NO<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>OC<sub>1-5</sub> alkyl, OH, SH,  
(CH<sub>2</sub>)<sub>r</sub>SC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>NR<sup>6f</sup>R<sup>6f</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

R<sup>6f</sup>, at each occurrence, is selected from H, C<sub>1-5</sub> alkyl,  
5 and C<sub>3-6</sub> cycloalkyl, and phenyl;

R<sup>6g</sup> is independently selected from -C(O)R<sup>6b</sup>, -C(O)OR<sup>6d</sup>,  
-C(O)NR<sup>6f</sup>R<sup>6f</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

10 R<sup>7</sup>, at each occurrence, is selected from C<sub>1-8</sub> alkyl, C<sub>2-8</sub>  
alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, Cl, Br,  
I, F, NO<sub>2</sub>, CN, (CR'R')<sub>r</sub>NR<sup>7a</sup>R<sup>7a</sup>, (CR'R')<sub>r</sub>OH,  
(CR'R')<sub>r</sub>O(CR'R')<sub>r</sub>R<sup>7d</sup>, (CR'R')<sub>r</sub>SH, (CR'R')<sub>r</sub>C(O)H,  
(CR'R')<sub>r</sub>S(CR'R')<sub>r</sub>R<sup>7d</sup>, (CR'R')<sub>r</sub>C(O)OH,  
15 (CR'R')<sub>r</sub>C(O)(CR'R')<sub>r</sub>R<sup>7b</sup>, (CR'R')<sub>r</sub>C(O)NR<sup>7a</sup>R<sup>7a</sup>,  
(CR'R')<sub>r</sub>NR<sup>7f</sup>C(O)(CR'R')<sub>r</sub>R<sup>7b</sup>, (CR'R')<sub>r</sub>C(O)O(CR'R')<sub>r</sub>R<sup>7d</sup>,  
(CR'R')<sub>r</sub>OC(O)(CR'R')<sub>r</sub>R<sup>7b</sup>,  
(CR'R')<sub>r</sub>OC(O)NR<sup>7a</sup>(CR'R')<sub>r</sub>R<sup>7a</sup>,  
(CR'R')<sub>r</sub>NR<sup>7a</sup>C(O)NR<sup>7a</sup>(CR'R')<sub>r</sub>R<sup>7a</sup>,  
20 (CR'R')<sub>r</sub>NR<sup>7f</sup>C(O)O(CR'R')<sub>r</sub>R<sup>7d</sup>, (CR'R')<sub>r</sub>C(=NR<sup>7f</sup>)NR<sup>7a</sup>R<sup>7a</sup>,  
(CR'R')<sub>r</sub>NHC(=NR<sup>7f</sup>)NR<sup>7f</sup>R<sup>7f</sup>, (CR'R')<sub>r</sub>S(O)<sub>p</sub>(CR'R')<sub>r</sub>R<sup>7b</sup>,  
(CR'R')<sub>r</sub>S(O)<sub>2</sub>NR<sup>7a</sup>R<sup>7a</sup>, (CR'R')<sub>r</sub>NR<sup>7a</sup>S(O)<sub>2</sub>NR<sup>7a</sup>R<sup>7a</sup>,  
(CR'R')<sub>r</sub>NR<sup>7f</sup>S(O)<sub>2</sub>(CR'R')<sub>r</sub>R<sup>7b</sup>, C<sub>1-6</sub> haloalkyl, C<sub>2-8</sub>  
alkenyl substituted with 0-3 R', C<sub>2-8</sub> alkynyl  
25 substituted with 0-3 R', and (CR'R')<sub>r</sub>phenyl  
substituted with 0-3 R<sup>7e</sup>;

alternatively, two R<sup>7</sup> on adjacent atoms on R<sup>2</sup> may join to  
form a cyclic acetal;

30

R<sup>7a</sup>, at each occurrence, is independently selected from H,  
methyl substituted with 0-1 R<sup>7g</sup>, C<sub>2-6</sub> alkyl  
substituted with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkenyl substituted

with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>7e</sup>,  
 a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub> carbocyclic residue substituted with  
 0-5 R<sup>7e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-10 membered heterocyclic  
 system containing 1-4 heteroatoms selected from N,  
 5 O, and S, substituted with 0-2 R<sup>7e</sup>;

R<sup>7b</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl  
 substituted with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkenyl substituted  
 with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>7e</sup>,  
 10 a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue substituted with 0-3  
 R<sup>7e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic system  
 containing 1-4 heteroatoms selected from N, O, and  
 S, substituted with 0-2 R<sup>7e</sup>;

15 R<sup>7d</sup>, at each occurrence, is selected from C<sub>3-8</sub> alkenyl  
 substituted with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkynyl substituted  
 with 0-2 R<sup>7e</sup>, methyl, CF<sub>3</sub>, C<sub>2-4</sub> haloalkyl, C<sub>2-6</sub> alkyl  
 substituted with 0-3 R<sup>7e</sup>, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub> carbocyclic  
 residue substituted with 0-3 R<sup>7e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6  
 20 membered heterocyclic system containing 1-4  
 heteroatoms selected from N, O, and S, substituted  
 with 0-3 R<sup>7e</sup>;

R<sup>7e</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub>  
 25 alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> cycloalkyl, Cl, F,  
 Br, I, CN, NO<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>OC<sub>1-5</sub> alkyl, OH, SH,  
 C(O)OC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>SC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>NR<sup>7f</sup>R<sup>7f</sup>, and  
 (CH<sub>2</sub>)<sub>r</sub>phenyl;

30 R<sup>7f</sup>, at each occurrence, is selected from H, C<sub>1-5</sub> alkyl,  
 and C<sub>3-6</sub> cycloalkyl, and phenyl;

R<sup>7g</sup> is independently selected from -C(O)R<sup>7b</sup>, -C(O)OR<sup>7d</sup>,  
 -C(O)NR<sup>7f</sup>R<sup>7f</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

R', at each occurrence, is selected from H, C<sub>1-6</sub> alkyl substituted with R<sup>6e</sup>, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, and (CH<sub>2</sub>)<sub>r</sub>phenyl substituted with R<sup>6e</sup>;

R<sup>8</sup> is selected from H, C<sub>1-4</sub> alkyl, and C<sub>3-4</sub> cycloalkyl;

R<sup>9</sup> is selected from H, C<sub>1-4</sub> alkyl, C<sub>3-4</sub> cycloalkyl, -C(O)H, and -C(O)-C<sub>1-4</sub>alkyl;

R<sup>10</sup> is independently selected from H, and C<sub>1-4</sub>alkyl substituted with 0-1 R<sup>10b</sup>;

R<sup>10b</sup>, at each occurrence, is independently selected from -OH, -SH, -NR<sup>10c</sup>R<sup>10c</sup>, -C(O)NR<sup>10c</sup>R<sup>10c</sup>, and -NHC(O)R<sup>10c</sup>;

R<sup>10c</sup> is selected from H, C<sub>1-4</sub> alkyl and C<sub>3-6</sub> cycloalkyl;

R<sup>11</sup> is selected from H, C<sub>1-4</sub> alkyl, (CHR)<sub>q</sub>OH, (CHR)<sub>q</sub>SH, (CHR)<sub>q</sub>OR<sup>11d</sup>, (CHR)<sub>q</sub>S(O)<sub>p</sub>R<sup>11d</sup>, (CHR)<sub>r</sub>C(O)R<sup>11b</sup>, (CHR)<sub>r</sub>NR<sup>11a</sup>R<sup>11a</sup>, (CHR)<sub>r</sub>C(O)NR<sup>11a</sup>R<sup>11a</sup>, (CHR)<sub>r</sub>C(O)NR<sup>11a</sup>OR<sup>11d</sup>, (CHR)<sub>q</sub>NR<sup>11a</sup>C(O)R<sup>11b</sup>, (CHR)<sub>q</sub>NR<sup>11a</sup>C(O)OR<sup>11d</sup>, (CHR)<sub>q</sub>OC(O)NR<sup>11a</sup>R<sup>11a</sup>, (CHR)<sub>r</sub>C(O)OR<sup>11d</sup>, a (CHR)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue substituted with 0-5 R<sup>11e</sup>, and a (CHR)<sub>r</sub>-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R<sup>11e</sup>;

R<sup>11a</sup>, at each occurrence, is independently selected from H, C<sub>1-4</sub> alkyl, C<sub>3-4</sub> alkenyl, C<sub>3-4</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue substituted with 0-5 R<sup>11e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered



heterocyclic system containing 1-4 heteroatoms  
selected from N, O, and S, substituted with 0-3 R<sup>11e</sup>;

R<sup>11b</sup>, at each occurrence, is independently selected from  
5 C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub>  
carbocyclic residue substituted with 0-2 R<sup>11e</sup>, and a  
(CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic system containing  
1-4 heteroatoms selected from N, O, and S,  
substituted with 0-3 R<sup>11e</sup>;

10

R<sup>11d</sup>, at each occurrence, is independently selected from  
H, methyl, -CF<sub>3</sub>, C<sub>2-4</sub> alkyl, C<sub>3-6</sub> alkenyl, C<sub>3-6</sub>  
alkynyl, a C<sub>3-6</sub> carbocyclic residue substituted with  
0-3 R<sup>11e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic  
15 system containing 1-4 heteroatoms selected from N,  
O, and S, substituted with 0-3 R<sup>11e</sup>;

R<sup>11e</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub>  
alkenyl, C<sub>2-8</sub> alkynyl, C<sub>3-6</sub> cycloalkyl, Cl, F, Br, I,  
20 CN, NO<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>OC<sub>1-5</sub> alkyl, OH, -O-C<sub>1-6</sub>  
alkyl, SH, (CH<sub>2</sub>)<sub>r</sub>SC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>NR<sup>11f</sup>R<sup>11f</sup>, and  
(CH<sub>2</sub>)<sub>r</sub>phenyl;

R<sup>11f</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl,  
25 and C<sub>3-6</sub> cycloalkyl;

R<sup>12</sup> is selected from H, C<sub>1-4</sub> alkyl, (CHR)<sub>q</sub>OH, (CHR)<sub>q</sub>SH,  
(CHR)<sub>q</sub>OR<sup>12d</sup>, (CHR)<sub>q</sub>S(O)<sub>p</sub>R<sup>12d</sup>, (CHR)<sub>r</sub>C(O)R<sup>12b</sup>,  
(CHR)<sub>r</sub>NR<sup>12a</sup>R<sup>12a</sup>, (CHR)<sub>r</sub>C(O)NR<sup>12a</sup>R<sup>12a</sup>,  
30 (CHR)<sub>r</sub>C(O)NR<sup>12a</sup>OR<sup>12d</sup>, (CHR)<sub>q</sub>NR<sup>12a</sup>C(O)R<sup>12b</sup>,  
(CHR)<sub>q</sub>NR<sup>12a</sup>C(O)OR<sup>12d</sup>, (CHR)<sub>q</sub>OC(O)NR<sup>12a</sup>R<sup>12a</sup>,

- (CHR)<sub>r</sub>C(O)OR<sup>12d</sup>, a (CHR)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue substituted with 0-5 R<sup>12e</sup>, and a (CHR)<sub>r</sub>-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R<sup>12e</sup>;
- 5 R<sup>12a</sup>, at each occurrence, is independently selected from H, C<sub>1-4</sub> alkyl, C<sub>3-4</sub> alkenyl, C<sub>3-4</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue substituted with 0-5 R<sup>12e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered
- 10 heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R<sup>12e</sup>;
- R<sup>12b</sup>, at each occurrence, is independently selected from C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub>
- 15 carbocyclic residue substituted with 0-2 R<sup>12e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R<sup>12e</sup>;
- 20 R<sup>12d</sup>, at each occurrence, is independently selected from H, methyl, -CF<sub>3</sub>, C<sub>2-4</sub> alkyl, C<sub>3-6</sub> alkenyl, C<sub>3-6</sub> alkynyl, a C<sub>3-6</sub> carbocyclic residue substituted with 0-3 R<sup>12e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic
- 25 system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R<sup>12e</sup>;
- R<sup>12e</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, C<sub>3-6</sub> cycloalkyl, Cl, F, Br, I, CN, NO<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>OC<sub>1-5</sub> alkyl, OH, -O-C<sub>1-6</sub>
- 30 alkyl, SH, (CH<sub>2</sub>)<sub>r</sub>SC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>NR<sup>12f</sup>R<sup>12f</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

$R^{12f}$ , at each occurrence, is selected from H,  $C_{1-6}$  alkyl, and  $C_{3-6}$  cycloalkyl;

5  $R^{13}$ , at each occurrence, is independently selected from H, and  $C_{1-4}$ alkyl substituted with 0-1  $R^{13b}$ , -OH, -NH<sub>2</sub>, F, Cl, Br, I, -OR<sup>13a</sup>, -N(R<sup>13a</sup>)<sub>2</sub>, and  $C_{1-4}$  alkyl substituted with 0-3  $R^{13b}$ ;

10  $R^{13a}$  is selected from H,  $C_{1-4}$  alkyl and  $C_{3-6}$  cycloalkyl;

$R^{13b}$ , at each occurrence, is independently selected from -OH, -SH, -NR<sup>13c</sup>R<sup>13c</sup>, -C(O)NR<sup>13c</sup>R<sup>13c</sup>, and -NHC(O)R<sup>13c</sup>;

15  $R^{13c}$  is selected from H,  $C_{1-4}$  alkyl and  $C_{3-6}$  cycloalkyl;

$R^{14}$ , at each occurrence, is independently selected from H and  $C_{1-4}$ alkyl;

20 alternatively, two  $R^{14}$ s, along with the carbon atom to which they are attached, join to form a  $C_{3-6}$  carbocyclic ring;

$R^{15}$ , at each occurrence, is independently selected from H,  
25  $C_{1-4}$ alkyl, OH, NH<sub>2</sub>, -O- $C_{1-4}$  alkyl, NR<sup>15a</sup>R<sup>15a</sup>,  
C(O)NR<sup>15a</sup>R<sup>15a</sup>, NR<sup>15a</sup>C(O)R<sup>15b</sup>, NR<sup>15a</sup>C(O)OR<sup>15d</sup>,  
OC(O)NR<sup>15a</sup>R<sup>15a</sup>, and (CHR)<sub>r</sub>C(O)OR<sup>15d</sup>;

alternatively, two  $R^{15}$ s, along with the carbon atom or  
30 atoms to which they are attached, join to form a  $C_{3-6}$  carbocyclic ring;

R<sup>15a</sup>, at each occurrence, is independently selected from  
H, and C<sub>1-4</sub> alkyl;

R<sup>15b</sup>, at each occurrence, is independently selected from  
5 C<sub>1-4</sub> alkyl, C<sub>3-6</sub> alkenyl, and C<sub>3-6</sub> alkynyl;

R<sup>15d</sup>, at each occurrence, is independently selected from  
C<sub>1-4</sub> alkyl, C<sub>3-6</sub> alkenyl, and C<sub>3-6</sub> alkynyl;

10 R<sup>16</sup> is selected from C<sub>1-4</sub> alkyl;

l is selected from 1, 2 and 3;

n is selected from 0, 1, 2, and 3;

15

m is selected from 0 and 1;

p, at each occurrence, is independently selected from 0,  
1, and 2;

20

q, at each occurrence, is independently selected from 1,  
2, 3, and 4;

r, at each occurrence, is independently selected from 0,  
25 1, 2, 3, and 4;

t, at each occurrence, is independently selected from 2,  
3, and 4;

30 s is selected from 0 and 1.

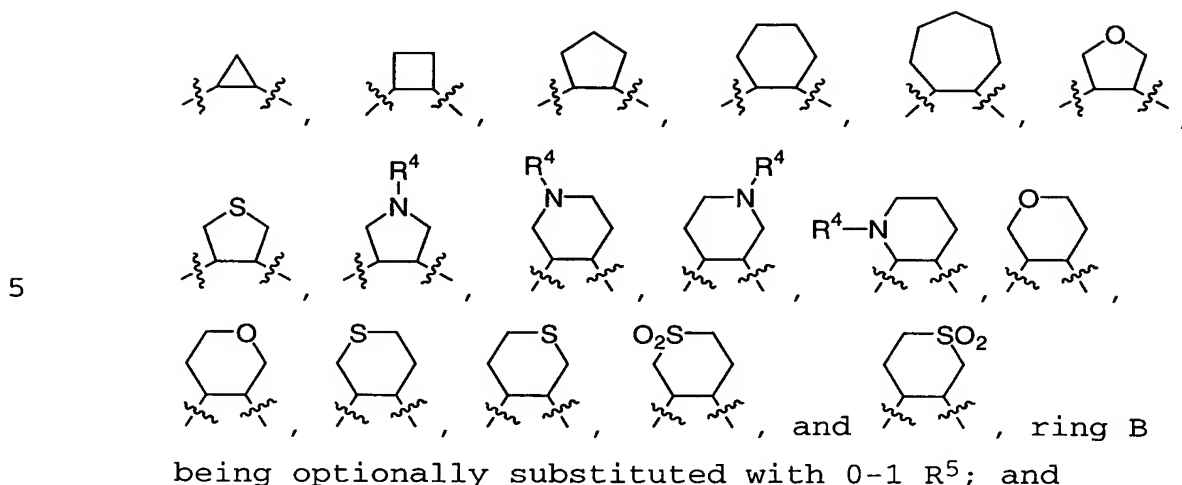
3. The compound of claim 2, wherein

m is 0.

35

4. The compound of claim 3, wherein:

ring B is selected from



R<sup>11</sup> and R<sup>12</sup> are H.

10

5. The compounds of claim 4, wherein:

R<sup>5</sup>, at each occurrence, is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CRR)<sub>r</sub>OH, (CRR)<sub>r</sub>SH, (CRR)<sub>r</sub>OR<sup>5d</sup>, (CRR)<sub>r</sub>SR<sup>5d</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>R<sup>5a</sup>, (CRR)<sub>r</sub>C(O)OH, (CRR)<sub>r</sub>C(O)R<sup>5b</sup>, (CRR)<sub>r</sub>C(O)NR<sup>5a</sup>R<sup>5a</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>C(O)R<sup>5b</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>C(O)OR<sup>5d</sup>, (CRR)<sub>r</sub>OC(O)NR<sup>5a</sup>R<sup>5a</sup>, (CHR)<sub>r</sub>NR<sup>5a</sup>C(O)NR<sup>5a</sup>R<sup>5a</sup>, CRR(CRR)<sub>r</sub>NR<sup>5a</sup>C(O)H, (CRR)<sub>r</sub>C(O)OR<sup>5b</sup>, (CRR)<sub>r</sub>OC(O)R<sup>5b</sup>, (CRR)<sub>r</sub>S(O)<sub>p</sub>R<sup>5b</sup>, (CRR)<sub>r</sub>S(O)<sub>2</sub>NR<sup>5a</sup>R<sup>5a</sup>, (CRR)<sub>r</sub>NR<sup>5a</sup>S(O)<sub>2</sub>R<sup>5b</sup>, and C<sub>1-6</sub> haloalkyl;

15

20

R<sup>5a</sup>, at each occurrence, is independently selected from H, methyl, C<sub>1-6</sub> alkyl substituted with 0-2 R<sup>5e</sup> wherein the alkyl is selected from ethyl, propyl, i-propyl, butyl, i-butyl, pentyl, hexyl, C<sub>3</sub> alkenyl substituted with 0-1 R<sup>5e</sup>, wherein the alkenyl is selected from allyl, C<sub>3</sub> alkynyl substituted with 0-1 R<sup>5e</sup> wherein

25

the alkynyl is selected from propynyl, and a  
 $(\text{CH}_2)_r\text{-C}_{3-4}$  carbocyclic residue substituted with 0-5  
 $\text{R}^{5e}$ , wherein the carbocyclic residue is selected from  
cyclopropyl, and cyclobutyl;

5

$\text{R}^{5b}$ , at each occurrence, is selected from  $\text{C}_{1-6}$  alkyl  
substituted with 0-2  $\text{R}^{5e}$ , wherein the alkyl is  
selected from methyl, ethyl, propyl, i-propyl,  
butyl, i-butyl, pentyl, and hexyl, a  $(\text{CH}_2)_r\text{-C}_{3-4}$   
10 carbocyclic residue substituted with 0-2  $\text{R}^{5e}$ , wherein  
the carbocyclic residue is selected from  
cyclopropyl, and cyclobutyl; and

$\text{R}^{5d}$ , at each occurrence, is selected from methyl,  $\text{CF}_3$ ,  
15  $\text{C}_{2-6}$  alkyl substituted with 0-2  $\text{R}^{5e}$ , wherein the  
alkyl is selected from methyl, ethyl, propyl,  
i-propyl, butyl, i-butyl, pentyl, and hexyl,  $\text{C}_{3-8}$   
alkenyl,  $\text{C}_{3-8}$  alkynyl, and a  $\text{C}_{3-10}$  carbocyclic  
residue substituted with 0-3  $\text{R}^{5e}$ .

20

6. The compound of claim 5, wherein:

$\text{R}^4$  is selected from H,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{3-8}$  alkenyl,  $\text{C}_{3-8}$   
alkynyl,  $(\text{CRR})_t\text{OH}$ ,  $(\text{CRR})_t\text{SH}$ ,  $(\text{CRR})_t\text{OR}^{4d}$ ,  $(\text{CRR})_t\text{SR}^{4d}$ ,  
25  $(\text{CRR})_t\text{NR}^{4a}\text{R}^{4a}$ ,  $(\text{CRR})_q\text{C}(\text{O})\text{OH}$ ,  $(\text{CRR})_r\text{C}(\text{O})\text{R}^{4b}$ ,  
 $(\text{CRR})_r\text{C}(\text{O})\text{NR}^{4a}\text{R}^{4a}$ ,  $(\text{CRR})_t\text{NR}^{4a}\text{C}(\text{O})\text{R}^{4b}$ ,  
 $(\text{CRR})_t\text{OC}(\text{O})\text{NR}^{4a}\text{R}^{4a}$ ,  $(\text{CRR})_t\text{NR}^{4a}\text{C}(\text{O})\text{OR}^{4d}$ ,  
 $(\text{CRR})_t\text{NR}^{4a}\text{C}(\text{O})\text{R}^{4b}$ ,  $(\text{CRR})_r\text{C}(\text{O})\text{OR}^{4b}$ ,  $(\text{CRR})_t\text{OC}(\text{O})\text{R}^{4b}$ ,  
 $(\text{CRR})_r\text{S}(\text{O})_p\text{R}^{4b}$ ,  $(\text{CRR})_r\text{S}(\text{O})_2\text{NR}^{4a}\text{R}^{4a}$ ,  $(\text{CRR})_r\text{NR}^{4a}\text{S}(\text{O})_2\text{R}^{4b}$ ;

30

R, at each occurrence, is independently selected from H,  
methyl, ethyl, propyl, allyl, propynyl,  $(\text{CH}_2)_r\text{C}_{3-6}$   
cycloalkyl, and  $(\text{CH}_2)_r\text{phenyl}$  substituted with  $\text{R}^{6e}$ ;

$R^5$ , at each occurrence, is independently selected from H,  
 methyl, ethyl, propyl, i-propyl, butyl, i-butyl,  
 allyl, propynyl,  $(CH_2)_rOH$ ,  $(CH_2)_rOR^{5d}$ ,  $(CH_2)_rNR^{5a}R^{5a}$ ,  
 $(CH_2)_rC(O)OH$ ,  $(CH_2)_rC(O)R^{5b}$ ,  $(CH_2)_rC(O)NR^{5a}R^{5a}$ ,  
 5  $(CH_2)_rNR^{5a}C(O)R^{5b}$ ,  $(CH_2)_rOC(O)NR^{5a}R^{5a}$ ,  
 $(CH_2)_rNR^{5a}C(O)OR^{5d}$ ,  $(CH_2)_rNR^{5a}C(O)R^{5b}$ ,  $(CH_2)_rC(O)OR^{5b}$ ,  
 $(CH_2)_rOC(O)R^{5b}$ ,  $(CH_2)_rNR^{5a}S(O)_2R^{5b}$ , and  $C_{1-6}$   
 haloalkyl;

10  $R^{5a}$ , at each occurrence, is independently selected from H,  
 methyl, ethyl, propyl, i-propyl, butyl, i-butyl,  
 pentyl, hexyl, cyclopropyl, and cyclobutyl; and

15  $r$ , at each occurrence, is selected from 0, 1, and 2.

7. The compound of claim 6, wherein:

$R^1$  is selected from phenyl substituted with 0-2  $R^6$ ,  
 naphthyl substituted with 0-2  $R^6$ , and a 5-10  
 20 membered heteroaryl system containing 1-4  
 heteroatoms selected from N, O, and S, substituted  
 with 0-3  $R^6$  wherein the heteroaryl is selected from  
 indolyl, benzimidazolyl, benzofuranyl,  
 benzothiofuranyl, benzoxazolyl, benzthiazolyl,  
 25 benzo[b]thiophene, benztriazolyl, benztetrazolyl,  
 benzisoxazolyl, benzisothiazolyl, benzimidazalonyl,  
 cinnolinyl, furanyl, imidazolyl, indazolyl, indolyl,  
 isoquinolinyl, isothiazolyl, isoxazolyl, oxazolyl,  
 pyrazinyl, pyrazolyl, pyridazinyl, pyridyl,  
 30 pyrido[2,3-d]pyrimidinyl, pyrimido[5,4-  
 d]pyrimidinyl, thieno[3,2-d]pyrimidinyl, pyridinyl,  
 pyrimidinyl, pyrrolyl, pyrrolo[2,1-  
 f][1,2,4]triazine, quinazolinyl, quinolinyl,  
 thiazolyl, thienyl, and tetrazolyl;

$R^2$  is selected from phenyl substituted with 0-2  $R^7$ , and a  
 5-10 membered heteroaryl system containing 1-4  
 heteroatoms selected from N, O, and S, substituted  
 5 with 0-3  $R^7$  wherein the heteroaryl is selected from  
 indolyl, benzimidazolyl, benzofuranyl,  
 benzothiofuranyl, benzoxazolyl, benzthiazolyl,  
 benzo[b]thiophene, benztriazolyl, benztetrazolyl,  
 benzisoxazolyl, benzisothiazolyl, benzimidazalonyl,  
 10 cinnolinyl, furanyl, imidazolyl, indazolyl, indolyl,  
 isoquinolinyl isothiazolyl, isoxazolyl, oxazolyl,  
 phthalazinyl, pyrazinyl, pyrazolyl, pyridazinyl,  
 pyridyl, pyrido[2,3-d]pyrimidinyl, thieno[3,2-  
 d]pyrimidinyl, pyridinyl, pyrimidinyl, pyrrolyl,  
 15 pyrrolo[2,1-f][1,2,4]triazine, quinazolinyl,  
 quinolinyl, thiazolyl, thienyl, and tetrazolyl;

$R^4$  is selected from H, methyl, ethyl, propyl, i-propyl,  
 butyl, i-butyl, allyl, propynyl,  $(CRR)_qOH$ ,  $(CRR)_tSH$ ,  
 20  $(CRR)_tOR^{4d}$ ,  $(CRR)_tSR^{4d}$ ,  $(CRR)_tNR^{4a}R^{4a}$ ,  $(CRR)_qC(O)OH$ ,  
 $(CRR)_rC(O)R^{4b}$ ,  $(CRR)_rC(O)NR^{4a}R^{4a}$ ,  $(CRR)_tNR^{4a}C(O)R^{4b}$ ,  
 $(CRR)_tOC(O)NR^{4a}R^{4a}$ ,  $(CRR)_tNR^{4a}C(O)OR^{4d}$ ,  
 $(CRR)_tNR^{4a}C(O)R^{4b}$ ,  $(CRR)_rC(O)OR^{4b}$ ,  $(CRR)_tOC(O)R^{4b}$ ,  
 $(CRR)_rS(O)_pR^{4b}$ ,  $(CRR)_rS(O)_2NR^{4a}R^{4a}$ ,  $(CRR)_rNR^{4a}S(O)_2R^{4b}$ ;

25  $R^{4a}$ , at each occurrence, is independently selected from H,  
 methyl substituted with 0-1  $R^{4c}$ ,  $C_{2-6}$  alkyl  
 substituted with 0-3  $R^{4e}$  wherein  $C_{2-6}$  is selected  
 from ethyl, propyl, i-propyl, butyl, i-butyl,  
 30 t-butyl, pentyl and hexyl, and a  $(CH_2)_r-C_{3-6}$   
 carbocyclic residue substituted with 0-4  $R^{4e}$  wherein  
 the carbocyclic residue is selected from  
 cyclopropyl, cyclohexyl, and phenyl;



R<sup>4b</sup> is selected from H, methyl, ethyl, propyl, i-propyl, butyl, i-butyl, t-butyl, pentyl, and cyclopropyl;

5 R<sup>4d</sup> is selected from methyl, ethyl, propyl, i-propyl, butyl, i-butyl, t-butyl, pentyl, and cyclopropyl; and

R<sup>8</sup> is selected from H, methyl, ethyl, propyl, i-propyl, and cyclopropyl.

10

8. The compound of claim 7, wherein:

R<sup>6</sup>, at each occurrence, is selected from C<sub>1-8</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CR'R')<sub>r</sub>C<sub>3-6</sub> cycloalkyl, Cl, Br, I, F, NO<sub>2</sub>, CN, (CR'R')<sub>r</sub>NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>OH, (CR'R')<sub>r</sub>O(CR'R')<sub>r</sub>R<sup>6d</sup>, (CR'R')<sub>r</sub>SH, (CR'R')<sub>r</sub>C(O)H, (CR'R')<sub>r</sub>S(CR'R')<sub>r</sub>R<sup>6d</sup>, (CR'R')<sub>r</sub>C(O)OH, (CR'R')<sub>r</sub>C(O)(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>C(O)NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>NR<sup>6f</sup>C(O)(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>C(O)O(CR'R')<sub>r</sub>R<sup>6d</sup>, (CR'R')<sub>r</sub>NR<sup>6a</sup>C(O)NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>NR<sup>6a</sup>C(S)NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>OC(O)(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>S(O)<sub>p</sub>(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>S(O)<sub>2</sub>NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>NR<sup>6f</sup>S(O)<sub>2</sub>(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>NR<sup>6f</sup>S(O)<sub>2</sub>NR<sup>6a</sup>R<sup>6a</sup>, C<sub>1-6</sub> haloalkyl, and (CR'R')<sub>r</sub>phenyl substituted with 0-3 R<sup>6e</sup>, and a (CH<sub>2</sub>)<sub>r-5-6</sub> membered heterocyclic system containing 1-2 heteroatoms selected from N, O, and S, substituted with 0-2 R<sup>6e</sup>;

30 R<sup>6a</sup>, at each occurrence, is independently selected from H, methyl, ethyl, propyl, i-propyl, butyl, i-butyl, t-butyl, pentyl, hexyl, cyclopropyl and phenyl;

35 R<sup>6b</sup>, at each occurrence, is selected from methyl, ethyl, propyl, i-propyl, butyl, i-butyl, t-butyl, pentyl, hexyl, cyclopropyl, and phenyl;

R<sup>6d</sup>, at each occurrence, is selected from methyl, CF<sub>3</sub>, ethyl, propyl, i-propyl, butyl, i-butyl, t-butyl, pentyl, hexyl, cyclopropyl, and phenyl;

5

R<sup>6e</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, Cl, F, Br, I, CN, NO<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>OC<sub>1-5</sub> alkyl, OH, SH, (CH<sub>2</sub>)<sub>r</sub>SC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>NR<sup>6f</sup>R<sup>6f</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

10

R<sup>6f</sup>, at each occurrence, is selected from H, methyl, ethyl, propyl, i-propyl, butyl, i-butyl, t-butyl, pentyl, hexyl, cyclopropyl, and phenyl;

15 R<sup>7</sup> is selected from methyl, ethyl, propyl, i-propyl, butyl, i-butyl, s-butyl, t-butyl, pentyl, hexyl, (CR'R')<sub>r</sub>C<sub>3-6</sub> cycloalkyl, Cl, Br, I, F, NO<sub>2</sub>, CN, (CR'R')<sub>r</sub>NR<sup>7a</sup>R<sup>7a</sup>, (CR'R')<sub>r</sub>OH, (CR'R')<sub>r</sub>O(CH)<sub>r</sub>R<sup>7d</sup>, (CR'R')<sub>r</sub>SH, (CR'R')<sub>r</sub>C(O)H, (CR'R')<sub>r</sub>S(CR'R')<sub>r</sub>R<sup>7d</sup>,  
 20 (CR'R')<sub>r</sub>C(O)OH, (CR'R')<sub>r</sub>C(O)(CR'R')<sub>r</sub>R<sup>7b</sup>, (CR'R')<sub>r</sub>C(O)NR<sup>7a</sup>R<sup>7a</sup>, (CR'R')<sub>r</sub>NR<sup>7f</sup>C(O)(CR'R')<sub>r</sub>R<sup>7b</sup>, (CR'R')<sub>r</sub>C(O)O(CR'R')<sub>r</sub>R<sup>7d</sup>, (CR'R')<sub>r</sub>OC(O)(CR'R')<sub>r</sub>R<sup>7b</sup>, (CR'R')<sub>r</sub>NR<sup>7a</sup>C(O)NR<sup>7a</sup>R<sup>7a</sup>, (CR'R')<sub>r</sub>NR<sup>7a</sup>C(O)O(CR'R')<sub>r</sub>R<sup>7d</sup>, (CR'R')<sub>r</sub>S(O)<sub>p</sub>(CR'R')<sub>r</sub>R<sup>7b</sup>, (CR'R')<sub>r</sub>S(O)<sub>2</sub>NR<sup>7a</sup>R<sup>7a</sup>,  
 25 (CR'R')<sub>r</sub>NR<sup>7f</sup>S(O)<sub>2</sub>(CR'R')<sub>r</sub>R<sup>7b</sup>, C<sub>1-6</sub> haloalkyl, and (CR'R')<sub>r</sub>phenyl substituted with 0-3 R<sup>7e</sup>;

R<sup>7a</sup>, at each occurrence, is selected from H, methyl, ethyl, propyl, i-propyl, butyl, i-butyl, t-butyl, pentyl, hexyl,, prop-2-enyl, 2-methyl-2-propenyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, CH<sub>2</sub>cyclopropyl, and benzyl;

30

R<sup>7b</sup>, at each occurrence, is selected from methyl, ethyl, propyl, i-propyl, butyl, i-butyl, t-butyl, pentyl,

35

hexyl, cyclopropyl, cyclopentyl, CH<sub>2</sub>-cyclopentyl, cyclohexyl, CH<sub>2</sub>-cyclohexyl, CF<sub>3</sub>, pyrrolidinyl, morpholinyl, piperizenyl substituted with 0-1 R<sup>7e</sup>, and azetidiny1;

5

R<sup>7d</sup>, at each occurrence, is selected from methyl, CF<sub>3</sub>, CF<sub>2</sub>CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, ethyl, propyl, i-propyl, butyl, i-butyl, t-butyl, pentyl, hexyl, and cyclopropyl;

10 R<sup>7e</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, Cl, F, Br, I, CN, NO<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>OC<sub>1-5</sub> alkyl, OH, SH, C(O)OC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>SC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>NR<sup>7f</sup>R<sup>7f</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

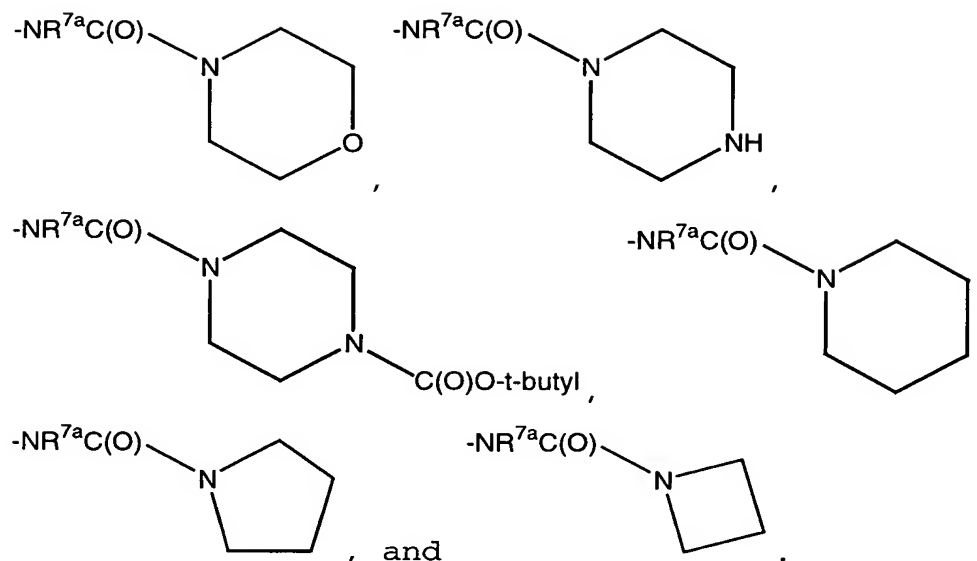
15

R<sup>7f</sup>, at each occurrence, is selected from H, methyl, ethyl, propyl, i-propyl, butyl, i-butyl, t-butyl, pentyl, hexyl, cyclopropyl, and phenyl; and

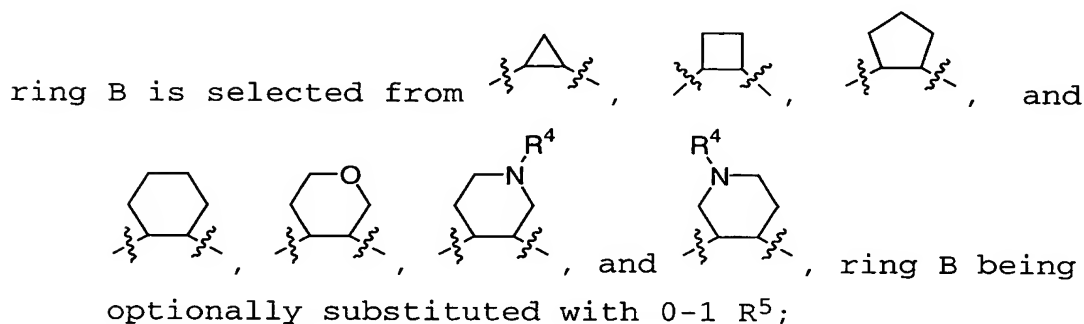
20 r is 0 or 1.

9. The compound of claim 8, wherein:

25 R<sup>7</sup> is selected from methyl, ethyl, propyl, i-propyl, butyl, i-butyl, s-butyl, pentyl, hexyl, Cl, Br, I, F, CN, NO<sub>2</sub>, NR<sup>7a</sup>R<sup>7a</sup>, NHC(O)NHR<sup>7a</sup>, NR<sup>7a</sup>C(O)R<sup>7b</sup>, NR<sup>7a</sup>C(O)OR<sup>7d</sup>, CF<sub>3</sub>, CF<sub>2</sub>CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, OCF<sub>3</sub>, C(O)R<sup>7b</sup>, C(O)OR<sup>7d</sup>, NR<sup>7f</sup>C(O)NR<sup>7a</sup>R<sup>7a</sup>, NHS(O)<sub>2</sub>R<sup>7b</sup>,



5            10. The compound of claim 9, wherein:



10

Z is selected from a bond, -NR<sup>8</sup>C(O)-, -C(O)NH-, and -NHC(O)NH-;

15            R<sup>1</sup> is selected from a C<sub>6-10</sub> aryl group substituted with 0-3 R<sup>6</sup> wherein the aryl group is selected from phenyl and naphthyl, and a 5-10 membered heteroaryl system containing 1-4 heteroatoms selected from N and O, substituted with 0-3 R<sup>6</sup> wherein the heteroaryl system is selected from indolyl, pyridinyl, pyrimidinyl, pyrido[2,3-d]pyrimidinyl, thieno[3,2-d]pyrimidinyl, imidazyolyl, and pyrrolyl

20            R<sup>2</sup> is phenyl substituted with 0-2 R<sup>7</sup>;

$R^4$  is selected from H, methyl, ethyl, propyl, i-propyl, butyl, i-butyl, t-butyl, pentyl, hexyl, and  $(CH_2)_r C(O)R^{4b}$ ;

5  $R^6$  is selected from methyl, ethyl, propyl, i-propyl, butyl, F, Cl, Br, I,  $NO_2$ , CN,  $O(CH_2)_r R^{6d}$ ,  $C(O)H$ ,  $C(O)R^{6d}$ ,  $C(O)OH$ ,  $SR^{6d}$ ,  $NR^{6a}R^{6a}$ ,  $NC(O)R^{6b}$ ,  $OC(O)R^{6b}$ ,  $S(O)_p R^{6b}$ ,  $(CHR')_r S(O)_2 NR^{6a}R^{6a}$ , and  $CF_3$ ;

10  $R^{6a}$  is H, methyl, or ethyl;

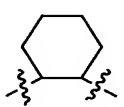
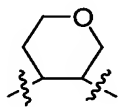
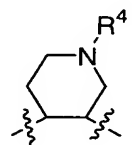
$R^{6b}$  is H, methyl, ethyl, propyl, i-propyl or butyl;

$R^{6d}$  is methyl, phenyl,  $CF_3$ , and  $(CH_2)$ -phenyl; and

15

$r$  is 0 or 1.

11. The compound of claim 10, wherein:

20 ring B is selected from , , and , ring B being substituted with 0-1  $R^5$ ;

25  $R^1$  is selected from a  $C_{6-10}$  aryl group substituted with 0-3  $R^6$  wherein the aryl group is selected from phenyl, and a 5-10 membered heteroaryl system containing 1-4 heteroatoms selected from N and O, substituted with 0-3  $R^6$  wherein the heteroaryl system is selected from indolyl and pyridinyl;

30  $R^4$  is selected from H, methyl, ethyl, propyl, i-propyl, butyl, i-butyl, t-butyl, pentyl, hexyl, allyl and  $(CH_2)_r C(O)R^{4b}$ ;

$R^5$  is selected from H, OH,  $OCH_3$ , and  $NR^{5a}R^{5a}$ ;

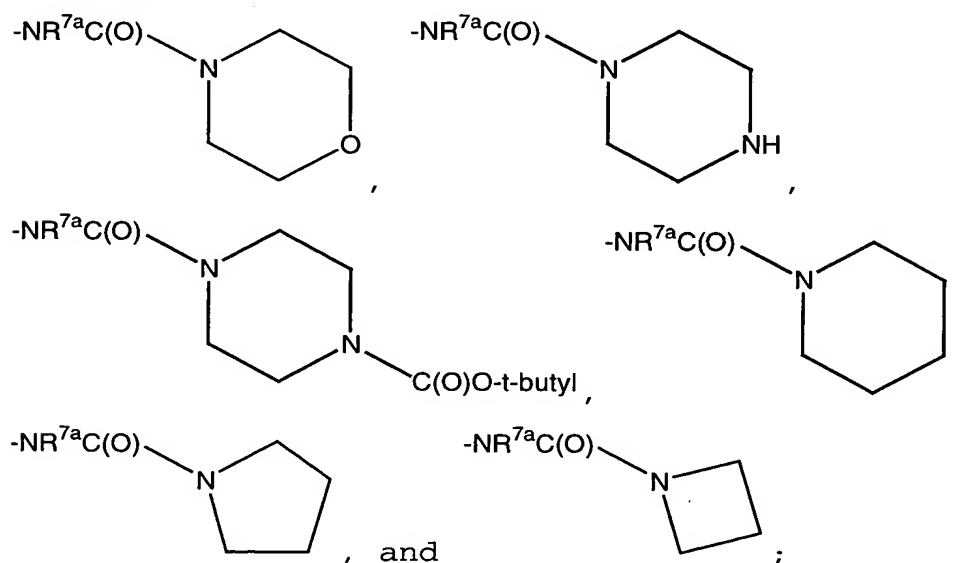
$R^{5a}$  is selected from H, methyl, ethyl, propyl, i-propyl, butyl, s-butyl, i-butyl, t-butyl, pentyl, hexyl, allyl, propargyl, cyclopropyl, cyclopropylmethyl, acetyl, methanesulfonyl,  $-C(O)CF_3$ ,  $C(=N)NH_2$ , benzyl, and  $-C(O)O-t\text{-butyl}$ ;

$R^6$  is selected from methyl, ethyl, propyl, i-propyl, butyl, vinyl, F, Cl, Br, I, CN,  $NR^{6a}R^{6a}$ ,  $C(O)H$ ,  $C(O)OH$ ,  $C(O)R^{6b}$ ,  $SR^{6d}$ ,  $S(O)_pR^{6d}$ ,  $S(O)_2NR^{6a}R^{6a}$ ,  $CF_3$ , and  $CH_2OH$ ;

$R^{6b}$  is H, methyl, ethyl, propyl, i-propyl or butyl;

$R^{6d}$  is methyl;

$R^7$  is selected from methyl, ethyl, propyl, i-propyl, butyl, i-butyl, s-butyl, pentyl, hexyl, Cl, Br, I, F, CN,  $NO_2$ ,  $NR^{7a}R^{7a}$ ,  $NHC(O)NHR^{7a}$ ,  $NR^{7a}C(O)R^{7b}$ ,  $NR^{7a}C(O)OR^{7d}$ ,  $CF_3$ ,  $CF_2CF_3$ ,  $CHF_2$ ,  $CH_2F$ ,  $OCF_3$ ,  $OCF_2CF_3$ ,  $OCHF_2$ , and  $OCH_2F$ ,  $C(O)OR^{7d}$ ,  $C(O)R^{7b}$ ,  $NR^{7f}C(O)NR^{7a}R^{7a}$ ,  $NHS(O)_2R^{7b}$ ,

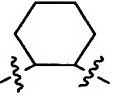


R<sup>7a</sup> is selected from H, methyl, ethyl, propyl, i-propyl,  
butyl, i-butyl, t-butyl, pentyl, neo-pentyl,  
cyclopropyl, cyclobutyl, cyclopentyl, and  
5 cyclohexyl;

R<sup>7b</sup> is selected from cyclohexyl and CF<sub>3</sub>; and

R<sup>7d</sup> is selected from methyl, ethyl, propyl, i-propyl,  
10 butyl, i-butyl, and t-butyl.

12. The compound of claim 11, wherein:

15 ring B is selected from , ring B being substituted  
with 0-1 R<sup>5</sup>;

R<sup>1</sup> is selected from a C<sub>6-10</sub> aryl group substituted with  
0-3 R<sup>6</sup> wherein the aryl group is phenyl;

20

R<sup>6</sup> is selected from methyl, ethyl, propyl, i-propyl, F,  
Cl, Br, CN, SCH<sub>3</sub>, and CF<sub>3</sub>;

R<sup>7</sup> is selected from methyl, ethyl, propyl, i-propyl,  
25 butyl, i-butyl, s-butyl, t-butyl, pentyl, hexyl,  
phenyl, adamantyl, benzyl, Cl, Br, I, F, CN, NO<sub>2</sub>,  
NR<sup>7a</sup>R<sup>7a</sup>, OR<sup>7d</sup>, NHC(O)NHR<sup>7a</sup>, NR<sup>7a</sup>C(O)R<sup>7b</sup>, NR<sup>7a</sup>C(O)OR<sup>7d</sup>,  
CF<sub>3</sub>, CF<sub>2</sub>CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, OCF<sub>3</sub>, OCF<sub>2</sub>CF<sub>3</sub>, OCHF<sub>2</sub>, and  
OCH<sub>2</sub>F, C(O)OR<sup>7d</sup>, C(O)R<sup>7b</sup>, and NR<sup>7f</sup>C(O)NR<sup>7a</sup>R<sup>7a</sup>;

30

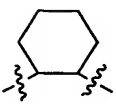
R<sup>7a</sup> is selected from H, methyl, ethyl, propyl, i-propyl,  
butyl, i-butyl, t-butyl, pentyl, neo-pentyl,  
cyclopropyl, cyclobutyl, cyclopentyl, and  
cyclohexyl.

13. The compound of claim 12, wherein

E is selected from  $-\text{CH}_2-\text{NH}-$ ,  $-\text{C}(\text{O})-\text{NH}-$  and  $-\text{SO}_2-\text{CH}_2-$ .

5

14. The compound of claim 1, wherein

B is , ring B being substituted with 0-1  $\text{R}^5$ ; and

10  $\text{R}^5$  is selected from H,  $\text{N}(\rightarrow\text{O})\text{R}^{5a}\text{R}^{5a}$ ,  $\text{N}_3$ ,  $\text{NR}^{5a}\text{C}(\text{O})\text{R}^{5b}$ ,  
 $\text{NR}^{5a}\text{C}(\text{O})\text{H}$ ,  $\text{NR}^{5a}\text{C}(\text{O})\text{OR}^{5d}$ ,  $\text{NR}^{5a}\text{C}(\text{O})\text{NR}^{5a}\text{R}^{5a}$ , and  $\text{NR}^{5a}\text{R}^{5a}$ ,  
 and a  $(\text{CH}_2)_r$ -5-6 membered heterocyclic system  
 containing 1-2 heteroatoms selected from N, O, and  
 S, substituted with 0-2  $\text{R}^{5e}$ , wherein the heterocyclic  
 15 system is selected from pyrrolidinyl, piperidinyl,  
 pyrrolidin-2-one, and isothiazolidine 1,1-dioxide.

15. The compound of claim 12, wherein

20 Z is selected from a bond,  $-\text{NR}^8\text{C}(\text{O})-$ ,  $-\text{C}(\text{O})\text{NH}-$ , and  
 $-\text{NHC}(\text{O})\text{NH}-$ .

16. The compound of claim 12, wherein

25  $\text{R}^6$  is selected from methyl, ethyl, propyl, i-propyl,  
 butyl, vinyl, F, Cl, Br, I,  $\text{C}(\text{O})\text{H}$ ,  $\text{C}(\text{O})\text{R}^{6b}$ ,  $\text{SR}^{6d}$ ,  
 $\text{S}(\text{O})_p\text{R}^{6d}$ ,  $\text{CF}_3$ , and  $\text{CH}_2\text{OH}$ ;

$\text{R}^{6b}$  is H, methyl, ethyl, propyl, i-propyl or butyl;

30

$\text{R}^{6d}$  is methyl;

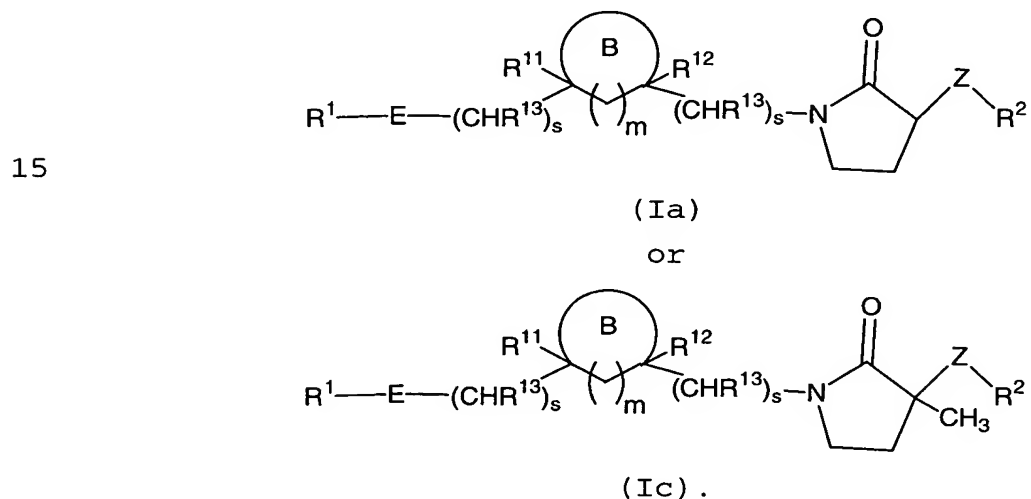


$R^7$  is selected from Cl, Br,  $NR^{7a}R^{7a}$ ,  $NR^{7a}C(O)OR^{7d}$ ,  
 $NHC(O)NHR^{7a}$ ,  $OCF_3$ , and  $CF_3$ ;

$R^{7a}$  is selected from H, methyl, ethyl, propyl, i-propyl,  
 5 butyl, i-butyl, t-butyl, pentyl, neo-pentyl,  
 cyclopropyl, cyclobutyl, cyclopentyl, and  
 cyclohexyl;

$R^{7d}$  is selected from methyl, ethyl, propyl, i-propyl,  
 10 butyl, i-butyl, and t-butyl.

17. The compound of claim 1, wherein the compound  
 is of formula (Ia) or (Ic)



18. The compound of claim 1, wherein the compound  
 is of formula (I) is selected:

25 2-{(3S)-1-[(1,2-cis)-2-(4-Methylsulfonyl-benzoylamino)-  
 cyclohexyl]-2-oxo-pyrrolidin-3-ylcarbamoyl}-4-  
 trifluoromethyl-phenyl)-carbamic acid tert-butyl  
 ester;

2-((3S)-1-[(1,2-cis)-2-(4-Methylsulfonyl-benzoylamino)-  
cyclohexyl]-2-oxo-pyrrolidin-3-ylcarbamoyl)-4-  
trifluoromethyl-phenyl)-amino;

5 N-((3S)-1-[(1S,2R,4R)-(Isopropyl-methyl-amino)-2-  
(toluene-4-sulfonylmethyl)-cyclohexyl]-2-oxo-  
pyrrolidin-3-yl)-3-trifluoromethyl-benzamide;

10 N-((3S)-1-[(1S,2R,4S)-(Isopropyl-methyl-amino)-2-  
(toluene-4-sulfonylmethyl)-cyclohexyl]-2-oxo-  
pyrrolidin-3-yl)-3-trifluoromethyl-benzamide;

15 N-((3S)-1-[(1S,2R,4R)-2-Benzenesulfonylmethyl-(isopropyl-  
methyl-amino)-cyclohexyl]-2-oxo-pyrrolidin-3-yl)-3-  
trifluoromethyl-benzamide;

20 N-((3S)-1-[(1S,2R,4S)-2-Benzenesulfonylmethyl-4-  
(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-  
pyrrolidin-3-yl)-3-trifluoromethyl-benzamide;

N-((3S)-1-[(1S,2R,4R)-2-Benzenesulfonylmethyl-4-  
(isopropyl-ethyl-amino)-cyclohexyl]-2-oxo-  
pyrrolidin-3-yl)-3-trifluoromethyl-benzamide;

25 N-((3S)-1-[(1S,2R,4S)-2-Benzenesulfonylmethyl-4-  
(isopropyl-ethyl-amino)-cyclohexyl]-2-oxo-  
pyrrolidin-3-yl)-3-trifluoromethyl-benzamide;

30 N-((3S)-1-[(1S,2R,4R)-2-Benzenesulfonylmethyl-4-  
(isopropyl-cyclopropylmethyl-amino)-cyclohexyl]-2-  
oxo-pyrrolidin-3-yl)-3-trifluoromethyl-benzamide;

(±) N-{(3S\*)-1-[(1S\*,2R\*,4R\*)-4-Azido-2-(4-methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-3-methyl-2-oxo-pyrrolidin-3-yl}-3-trifluoromethyl-benzamide;

5

(±) N-{(3S\*)-1-[(1S\*,2R\*,4R\*)-4-Amino-2-(4-methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-3-methyl-2-oxo-pyrrolidin-3-yl}-3-trifluoromethyl-benzamide;

10

(±) N-{(3S\*)-1-[(1S\*,2R\*,4R\*)-4-Isopropylamino-2-(4-methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-3-methyl-2-oxo-pyrrolidin-3-yl}-3-trifluoromethyl-benzamide;

15

(±) N-{(3S\*)-1-[(1S\*,2R\*,4R\*)-4-(Isopropyl-methyl-amino)-2-(4-methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-3-methyl-2-oxo-pyrrolidin-3-yl}-3-trifluoromethyl-benzamide;

20

(±) N-{(3S\*)-1-[(1S\*,2R\*,4R\*)-4-(Isopropyl-prop-2-ynyl-amino)-2-(4-methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-3-methyl-2-oxo-pyrrolidin-3-yl}-3-trifluoromethyl-benzamide;

25

(±) N-{(3S\*)-1-[(1S\*,2R\*,4R\*)-4-(Cyclopropylmethyl-isopropyl-amino)-2-(4-methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-3-methyl-2-oxo-pyrrolidin-3-yl}-3-trifluoromethyl-benzamide;

30

N-{(3S)-1-[4-(Isopropyl-methyl-amino)-2-(4-methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-2-

oxo-pyrrolidin-3-yl}-N-methyl-3-trifluoromethyl-  
benzamide;

5 N-((3S)-1-[(1S,2R,4R)-4-(Isopropyl-methyl-amino)-2-(4-  
methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-2-  
oxo-pyrrolidin-3-yl)-3-trifluoromethyl-benzamide;

10 1-((3S)-1-[(1S,2R,4R)-4-(Isopropyl-methyl-amino)-2-(4-  
methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-2-  
oxo-pyrrolidin-3-yl)-3-(3-trifluoromethyl-phenyl)-  
urea;

15 N-((3S)-1-[(1S,2R,4R)-4-(Isopropyl-methyl-amino)-2-(4-  
methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-2-  
oxo-pyrrolidin-3-yl)-3-trifluoromethyl-  
benzenesulfonamide;

20 N-((3S)-1-[(1S,2R,4R)-4-(Isopropyl-methyl-amino)-2-(4-  
methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-2-  
oxo-pyrrolidin-3-yl)-benzamide;

25 { (3S)-1-[(1S,2R,4R)-2-Benzenesulfonylmethyl-4-(isopropyl-  
methyl-amino)-cyclohexyl]-2-oxo-pyrrolidin-3-yl}-3-  
(3-trifluoromethyl-phenyl)-urea;

N-[(3S)-1-((1S,2R,4R)-2-Benzenesulfonylmethyl-4-  
isopropylamino-cyclohexyl)-2-oxo-pyrrolidin-3-yl]-3-  
trifluoromethyl-benzamide;

30 N-((3S)-1-[(1S,2R,4R)-4-(Allyl-isopropyl-amino)-2-  
benzenesulfonylmethyl-cyclohexyl]-2-oxo-pyrrolidin-  
3-yl)-3-trifluoromethyl-benzamide;

- 1-((1S,2R)-2-Benzenesulfonylmethyl-4-isopropylamino-cyclohexyl)-2-oxo-pyrrolidine-3-carboxylic acid (3-trifluoromethyl-phenyl)-amide;
- 5 1-((1S,2R)-2-Benzenesulfonylmethyl-4-isopropylamino-cyclohexyl)-2-oxo-pyrrolidine-3-carboxylic acid (3-trifluoromethyl-phenyl)-amide;
- 10 (2-((3S)-1-[(1S,2R)-2-(4-Methylsulfanyl-benzylamino)-cyclohexyl]-2-oxo-pyrrolidin-3-ylcarbonyl)-4-trifluoromethyl-phenyl)-carbamic acid tert-butyl ester;
- 15 N-((3S)-1-[(1S,2R,4R)-2-Benzenesulfonylmethyl-4(R)-(isopropyl-propyl-amino)-cyclohexyl]-2-oxo-pyrrolidin-3-yl)-3-trifluoromethyl-benzamide;
- 20 (±) 1-[(1S\*,2R\*,4R\*)-4-Isopropylamino-2-(4-methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-4-(3-trifluoromethyl-phenyl)-5,6-dihydro-1H-pyridin-2-one;
- 25 (±) 1-[(1S\*,2R\*,4R\*)-4-Isopropylamino-2-(4-benzenesulfonylmethyl)-cyclohexyl]-4-(3-trifluoromethyl-phenyl)-5,6-dihydro-1H-pyridin-2-one;
- 30 (±) 1-[(1S\*,2R\*,4R\*)-4-Isopropylmethylamino-2-(4-methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-4-(3-trifluoromethyl-phenyl)-5,6-dihydro-1H-pyridin-2-one;

- (±) 1-[(1S\*,2R\*,4R\*)-4-Amino-2-(4-methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-4-(3-trifluoromethoxyphenyl)-5,6-dihydro-1H-pyridin-2-one;
- 5
- (±) 1-[(1S\*,2R\*,4R\*)-4-Isopropylamino-2-(4-methylsulfanyl-benzenesulfonylmethyl)-cyclohexyl]-4-(3-trifluoromethoxyphenyl)-5,6-dihydro-1H-pyridin-2-one;
- 10
- (±) 1-[(1S\*,2R\*,4R\*)-4-Isopropylamino-2-(4-benzenesulfonylmethyl)-cyclohexyl]-4-(3-trifluoromethyl-phenyl)-piperidin-2-one;
- 15
- (S)-3-(3-(trifluoromethyl)benzylamino)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(4-(methylthio)phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;
- 20
- 3(R)-(3-(trifluoromethyl)phenethyl)-1-((1S,2R,4R/S)-4-(isopropylamino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one trifluoroacetate
- 25
- 3(S)-(3-(Trifluoromethyl)phenethyl)-1-((1S,2R,4R/S)-4-(isopropylamino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one trifluoroacetate
- 30
- N-((S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxoazepan-3-yl)-3-(trifluoromethyl)benzamide;

N-((S)-1-((1S,2R,4R)-4-(dimethylamino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopiperidin-3-yl)-3-(trifluoromethyl)benzamide;

5 (R\*)-1-((1S\*,2R\*,4R\*)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-((2-(3-(trifluoromethyl)phenyl)-1,3-dioxolan-2-yl)methyl)pyrrolidin-2-one;

10 (S\*)-1-((1S\*,2R\*,4R\*)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-((2-(3-(trifluoromethyl)phenyl)-1,3-dioxolan-2-yl)methyl)pyrrolidin-2-one;

15 (S\*)-3-(2-oxo-2-(3-(trifluoromethyl)phenyl)ethyl)-1-((1S\*,2R\*,4R\*)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;

(R\*)-3-(2-oxo-2-(3-(trifluoromethyl)phenyl)ethyl)-1-  
20 ((1S\*,2R\*,4R\*)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;

(R\*)-3-(2-hydroxy-2-(3-(trifluoromethyl)phenyl)ethyl)-1-  
25 ((1S\*,2R\*,4R\*)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;

(S\*)-3-(2-hydroxy-2-(3-(trifluoromethyl)phenyl)ethyl)-1-  
((1S\*,2R\*,4R\*)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;

30

((S\*)-1-((1S\*,2R\*,4R\*)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(-2-(methoxyimino)-2-(3-(trifluoromethyl)phenyl)ethyl)pyrrolidin-2-one;

35

((R\*)-1-((1S\*,2R\*,4R\*)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(-2-(methoxyimino)-2-(3-(trifluoromethyl)phenyl)ethyl)pyrrolidin-2-one;

5

1-((1S\*,2R\*,4R\*)-4-(amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(7-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)pyrrolidin-2-one;

10

1-((1S\*,2R\*,4R\*)-4-(isopropylamino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(7-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)pyrrolidin-2-one;

15

1-((1S\*,2R\*,4R\*)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(7-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)pyrrolidin-2-one;

20

1-((1S\*,2R\*,4R\*)-4-(isopropyl(ethyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(7-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)pyrrolidin-2-one;

25

1-((1S\*,2R\*,4R\*)-4-(Diethylamino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(7-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)pyrrolidin-2-one;

30

1-((1S,2R,4R)-4-(Isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(naphthalen-1-ylamino)pyrrolidin-2-one;



- 3-(Benzo[b]thiophen-3-ylamino)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;
- 5 (S)-3-(6-chloroquinazolin-4-ylamino)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;
- (S)-3-(6,8-dichloroquinazolin-4-ylamino)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;
- 10
- 3,5-Dichloro-N-((S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)benzamide;
- 15
- N-((S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)-3-(trifluoromethoxy)benzamide;
- 20
- 3-((E)-3(R\*)-(trifluoromethyl)styryl)-1-((1S\*,2R\*,4R\*)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;
- 25
- 1-((1S\*,2R\*,4R\*)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3(R\*)-((E/Z)-2-(3-(trifluoromethyl)phenyl)prop-1-enyl)pyrrolidin-2-one;
- 30
- N-(1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3(R)-yl)benzamide;

N-((S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)-3,5-bis(trifluoromethyl)benzamide;

5 2-Amino-N-(1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3(R)-yl)-5-(trifluoromethoxy)benzamide;

10 (R)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(6-(trifluoromethyl)quinolin-4-ylamino)pyrrolidin-2-one;

15 (S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(6-(trifluoromethyl)quinolin-4-ylamino)pyrrolidin-2-one;

20 (R)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(7-(trifluoromethyl)quinolin-4-ylamino)pyrrolidin-2-one;

25 (S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(7-(trifluoromethyl)quinolin-4-ylamino)pyrrolidin-2-one;

30 3-(2-(Phenyl)phenylamino)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;

- 3-(3,5-Bis(trifluoromethyl)phenylamino)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;
- 5 1-((1S,2R,4R)-4-(Isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(2-(trifluoromethyl)phenylamino)pyrrolidin-2-one;
- 10 1-((1S,2R,4R)-4-(Isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(2-methoxyphenylamino)pyrrolidin-2-one;
- 15 1-((1S,2R,4R)-4-(Isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(3-(trifluoromethyl)phenylamino)pyrrolidin-2-one;
- 20 1-((1S,2R,4R)-4-(Isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(4-(trifluoromethyl)phenylamino)pyrrolidin-2-one;
- 3-Chloro-N-((S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)benzamide;
- 25 3-Fluoro-N-((S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)-5-(trifluoromethyl)benzamide;
- 30 tert-Butyl (1R,3R,4S)-4-((S)-2-oxo-3-(3-(trifluoromethyl)benzamido)pyrrolidin-1-yl)-3-(phenylsulfonylmethyl)cyclohexylcarbamate;

- N-((S)-2-Oxo-1-((1S,2R,4R)-4-(phenylamino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-3-yl)-3-(trifluoromethyl)benzamide;
- 5 N-(2-Oxo-1-((1S,2R,4R)-2-(phenylsulfonylmethyl)-4-(pyridin-4-ylamino)cyclohexyl)pyrrolidin-3-yl)-3-(trifluoromethyl)benzamide;
- 10 N-(2-Oxo-1-((1S,2R,4R)-2-(phenylsulfonylmethyl)-4-(thiazol-2-ylamino)cyclohexyl)pyrrolidin-3-yl)-3-(trifluoromethyl)benzamide;
- 15 Methyl (1R,3R,4S)-4-((S)-2-oxo-3-(3-(trifluoromethyl)benzamido)pyrrolidin-1-yl)-3-(phenylsulfonylmethyl)cyclohexylcarbamate;
- 20 N-((S)-1-((1S,2R,4R)-4-Formamido-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)-3-(trifluoromethyl)benzamide;
- 1-((1R,3R,4S)-4-((S)-2-Oxo-3-(3-(trifluoromethyl)benzamido)pyrrolidin-1-yl)-3-(phenylsulfonylmethyl)cyclohexyl)urea;
- 25 1-Methyl-3-((1R,3R,4S)-4-((S)-2-oxo-3-(3-(trifluoromethyl)benzamido)pyrrolidin-1-yl)-3-(phenylsulfonylmethyl)cyclohexyl)urea;
- 30 N-((S)-2-Oxo-1-((1S,2R,4R)-4-(2-oxopyrrolidin-1-yl)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-3-yl)-3-(trifluoromethyl)benzamide;

- N-((S)-1-((1S,2R,4R)-4-(1,1-dioxido-isothiazolidin-2-yl)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)-3-(trifluoromethyl)benzamide;
- 5 N-((S)-1-((1S,2R,4R)-2-((4-Chlorophenylsulfonyl)methyl)-4-(isopropyl(methyl)amino)cyclohexyl)-2-oxopyrrolidin-3-yl)-3-fluoro-5-(trifluoromethyl)benzamide;
- 10 3-Chloro-N-((S)-1-((1S,2R,4R)-2-((4-chlorophenylsulfonyl)methyl)-4-(isopropyl(methyl)amino)cyclohexyl)-2-oxopyrrolidin-3-yl)benzamide;
- 15 N-((S)-1-((1S,2R,4R)-2-((4-chlorophenylsulfonyl)methyl)-4-(isopropyl(methyl)amino)cyclohexyl)-2-oxopyrrolidin-3-yl)-3,5-bis(trifluoromethyl)benzamide;
- 20 tert-Butyl 2-(((S)-1-((1S,2R,4R)-2-((4-chlorophenylsulfonyl)methyl)-4-(isopropyl(methyl)amino)cyclohexyl)-2-oxopyrrolidin-3-yl)carbamoyl)-4-(trifluoromethoxy)phenylcarbamate;
- 25 2-Amino-N-((S)-1-((1S,2R,4R)-2-((4-chlorophenylsulfonyl)methyl)-4-(isopropyl(methyl)amino)cyclohexyl)-2-oxopyrrolidin-3-yl)-5-(trifluoromethoxy)benzamide;
- 30 N-((S)-1-((1S,2R,4R)-2-((4-Chlorophenylsulfonyl)methyl)-4-(isopropyl(methyl)amino)cyclohexyl)-2-oxopyrrolidin-3-yl)-3-(trifluoromethoxy)benzamide;

- N-((S)-1-((1S,2R,4R)-2-((4-Chlorophenylsulfonyl)methyl)-4-(isopropyl(methyl)amino)cyclohexyl)-2-oxopyrrolidin-3-yl)-3-(trifluoromethyl)benzamide;
- 5 3,5-Dichloro-N-((S)-1-((1S,2R,4R)-2-((4-chlorophenylsulfonyl)methyl)-4-(isopropyl(methyl)amino)cyclohexyl)-2-oxopyrrolidin-3-yl)benzamide;
- 10 3-Chloro-N-((S)-1-((1S,2R,4R)-2-((4-chlorophenylsulfonyl)methyl)-4-(isopropyl(methyl)amino)cyclohexyl)-2-oxopyrrolidin-3-yl)benzamide N-Oxide;
- 15 N-((S)-1-((1S,2R,4R)-2-((4-Chlorophenylsulfonyl)methyl)-4-(isopropyl(methyl)amino)cyclohexyl)-2-oxopyrrolidin-3-yl)-3-(trifluoromethyl)benzamide N-Oxide;
- 20 N-((S)-1-((1S,2R,4R)-2-((4-Chlorophenylsulfonyl)methyl)-4-(isopropyl(methyl)amino)cyclohexyl)-2-oxopyrrolidin-3-yl)-3-fluoro-5-(trifluoromethyl)benzamide N-Oxide;
- 25 N-((S)-1-((1S,2R,4R)-4-(Isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)-3-(trifluoromethyl)benzamide N-Oxide;
- 30 N-((S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-((4-isopropylphenylsulfonyl)methyl)cyclohexyl)-2-oxopyrrolidin-3-yl)-3-(trifluoromethyl)benzamide;

- N-((S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(o-tolylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)-3-(trifluoromethyl)benzamide;
- 5 N-((S)-1-((1S,2R,4R)-2-((4-Fluorophenylsulfonyl)methyl)-4-(isopropyl(methyl)amino)cyclohexyl)-2-oxopyrrolidin-3-yl)-3-(trifluoromethyl)benzamide;
- 10 3-Chloro-N-((S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(tosylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)benzamide;
- 15 2-Amino-N-((S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(tosylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)-5-(trifluoromethoxy)benzamidemide;
- 20 1-[(1S, 2R, 4R)-(4-Amino-2-benzenesulfonylmethylcyclohexyl)-4-(3-trifluoromethylphenyl)]-5,6-dihydro-1H-pyridin-2-one;
- 1-([(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-isopropylamino-cyclohexyl)-4-(3-trifluoromethylphenyl)]-5,6-dihydro-1H-pyridin-2-one;
- 25 1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropylmethyl-amino)cyclohexyl]-4-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyridin-2-one;
- 30 1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropylethyl-amino)cyclohexyl]-4-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyridin-2-one;
- 1-[1S, 2R, 4R)-2-Benzenesulfonylmethyl-4-(isopropylmethyl-amino)-cyclohexyl]- (3S)-3-(6-chloro-2-

trifluoromethyl-quinazolin-4-ylamino)-pyrrolidin-2-one;

1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-  
5 methyl-amino)-cyclohexyl]-(3S)-3-(7-chloro-  
quinazolin-4-ylamino)-pyrrolidin-2-one;

1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-  
methyl-amino)-cyclohexyl]-(3S)-3-(2,6-dichloro-  
10 quinazolin-4-ylamino)-pyrrolidin-2-one;

1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-  
methyl-amino)-cyclohexyl]-(3S)-3-(6-chloro-2-  
dimethylamino-quinazolin-4-ylamino)-pyrrolidin-2-  
15 one;

1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-  
methyl-amino)-cyclohexyl]-(3S)-3-(6-chloro-2-  
hydroxy-quinazolin-4-ylamino)-pyrrolidin-2-one;  
20

1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-  
methyl-amino)-cyclohexyl]-(3S)-3-(6-trifluoromethyl-  
quinazolin-4-ylamino)-pyrrolidin-2-one;

25 1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-  
methyl-amino)-cyclohexyl]-(3S)-3-(6-tert-butyl-  
thieno[3,2-d]pyrimidin-4-ylamino)-pyrrolidin-2-one;

1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-  
30 methyl-amino)-cyclohexyl]-(3S)-3-(6-tert-butyl-2-  
trifluoromethyl-thieno[3,2-d]pyrimidin-4-ylamino)-  
pyrrolidin-2-one;



1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-(3S)-3-(6-tert-butyl-pyrrolo[2,1-f][1,2,4]triazin-4-ylamino)-pyrrolidin-2-one;

5

(3S)-3-(6-Adamantan-1-yl-pyrrolo[2,1-f][1,2,4]triazin-4-ylamino)-1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-pyrrolidin-2-one;

10

3-Methyl-2-phenyl-3H-imidazole-4-carboxylic acid {(3S)-1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-pyrrolidin-3-yl}-amide;

15

1-Methyl-2-phenyl-1H-imidazole-4-carboxylic acid {(3S)-1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-pyrrolidin-3-yl}-amide;

20

3-Benzyl-2-phenyl-3H-imidazole-4-carboxylic acid {(3S)-1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-pyrrolidin-3-yl}-amide;

25

1-Benzyl-2-phenyl-1H-imidazole-4-carboxylic acid {(3S)-1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-pyrrolidin-3-yl}-amide;

30

2-Phenyl-3H-imidazole-4-carboxylic acid {(3S)-1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-pyrrolidin-3-yl}-amide;

Preparation of 1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-(3S)-3-(6,7-dimethoxy-quinazolin-4-ylamino)-pyrrolidin-2-one;

5

1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-(3S)-3-(6-fluoro-quinazolin-4-ylamino)-pyrrolidin-2-one;

10 1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-(3S)-3-(6-methyl-quinazolin-4-ylamino)-pyrrolidin-2-one;

1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-(3S)-3-(6-phenyl-thieno[2,3-d]pyrimidin-4-ylamino)-pyrrolidin-2-one;

15

1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-(3S)-3-(6-chloro-2-propyl-pyrido[2,3-d]pyrimidin-4-ylamino)-pyrrolidin-2-one;

20

1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-(3S)-3-(6-chloro-2-isopropyl-quinazolin-4-ylamino)-pyrrolidin-2-one;

25

1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-(3S)-3-(2-tert-butyl-6-chloro-quinazolin-4-ylamino)-pyrrolidin-2-one;

30 1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-(3S)-3-(6-chloro-2-methyl-quinazolin-4-ylamino)-pyrrolidin-2-one;

- 1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-(3S)-3-(6-chloro-2-ethyl-quinazolin-4-ylamino)-pyrrolidin-2-one;
- 5 N-[(3S)-1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-2,5-dioxo-pyrrolidin-3-yl]-3-trifluoromethyl-benzamide;
- 10 N-[(3S)-1-[-(1S, 2R, 4R)-2-Benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-pyrrolidin-3-yl]-4-adamantan-1-yl-1H-pyrrole-2-carboxamide;
- 15 N-[(3S)-1-[-(1S, 2R, 4R)-2-Benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-pyrrolidin-3-yl]-4-adamantan-1-yl-1-methyl-1H-pyrrole-2-carboxamide;
- 20 1-[(1S, 2R, 4R)-2-Benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-(3S)-3-(6-tert-butyl-pyrimido[5,4-d]pyrimidin-4-ylamino)-pyrrolidin-2-one;
- 25 5-Bromo-2-tert-butyl-pyrimidine-4-carboxylic acid {(3S)-1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-pyrrolidin-3-yl}-amide;
- 30 2-tert-Butyl-pyrimidine-4-carboxylic acid {(3S\*)-1-[(1S\*, 2R\*, 4R\*)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-pyrrolidin-3-yl}-amide;

2-tert-Butyl-5-phenyl-pyrimidine-4-carboxylic acid {(3S)-  
1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-  
(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-  
pyrrolidin-3-yl}-amide;

5

N-[(3S)-1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-  
(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-  
pyrrolidin-3-yl]-3-tert-butyl-benzamide;

10 N-[(3S)-1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-  
(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-  
pyrrolidin-3-yl]-3-bromo-5-tert-butyl-benzamide;

15 1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-  
methyl-amino)-cyclohexyl]-(3S)-3-(pyrido[2,3-  
d]pyrimidin-4-ylamino)-pyrrolidin-2-one;

20 1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-  
methyl-amino)-cyclohexyl]-(3S)-3-(6-chloro-  
pyrido[2,3-d]pyrimidin-4-ylamino)-pyrrolidin-2-one;

25 1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-  
methyl-amino)-cyclohexyl]-(3S)-3-(6-chloro-2-  
trifluoromethyl-pyrido[2,3-d]pyrimidin-4-ylamino)-  
pyrrolidin-2-one;

30 1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-  
methyl-amino)-cyclohexyl]-(3S)-3-(6-  
trifluoromethoxy-pyrido[2,3-d]pyrimidin-4-ylamino)-  
pyrrolidin-2-one;

- 1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-(3S)-3-(6-chloro-2-methylamino-quinazolin-4-ylamino)-pyrrolidin-2-one;
- 5 (3S)-3-(6-Fluoro-quinazolin-4-ylamino)-1-[(1S, 2R, 4R)-4-(isopropyl-methyl-amino)-2-(toluene-4-sulfonylmethyl)-cyclohexyl]-pyrrolidin-2-one;
- 10 N-{1-[(1S, 2R, 4R)-2-benzenesulfonylmethyl-4-(isopropyl-methyl-amino)-cyclohexyl]-2-oxo-pyrrolidin-(3S)-3-yl}-2-chloro-5-trifluoromethyl-benzamide;
- (S)-3-(6-Bromoquinazolin-4-ylamino)-1-((1S, 2R, 4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;
- 15 (S)-3-(6,7-Difluoroquinazolin-4-ylamino)-1-((1S, 2R, 4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;
- 20 (S)-3-(6-Methoxyquinazolin-4-ylamino)-1-((1S, 2R, 4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;
- 25 ((S)-1-((1S, 2R, 4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-3-(quinazolin-4-ylamino)pyrrolidin-2-one;
- 30 3-Phenyl-N-((S)-1-((1S, 2R, 4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)benzamide;

(S)-3-(6-Iodoquinazolin-4-ylamino)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)pyrrolidin-2-one;

5 3-Tert-butyl-4-hydroxy-N-((S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)benzamide;

10 3-Amino-5-tert-butyl-N-((S)-1-((1S,2R,4R)-4-(isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)thiophene-2-carboxamide;

15 N-((S)-1-((1S,2R,4R)-4-(Isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)-2-methyl-5-phenylfuran-3-carboxamide;

20 N-((S)-1-((1S,2R,4R)-4-(Isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)-5-nitrofuran-2-carboxamide; and

25 N-((S)-1-((1S,2R,4R)-4-(Isopropyl(methyl)amino)-2-(phenylsulfonylmethyl)cyclohexyl)-2-oxopyrrolidin-3-yl)-4-phenylthiophene-2-carboxamide.

19. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 1.

30

20. A method for modulation of chemokine receptor activity comprising administering to a patient in need thereof a therapeutically effective amount of a compound of claim 1.

21. A method for modulation of MCP-1, MCP-2, MCP-3  
and MCP-4, and MCP-5 activity that is mediated by the  
CCR2 receptor comprising administering to a patient in  
5 need thereof a therapeutically effective amount of a  
compound of claim 1.

22. A method for modulation of MCP-1 activity  
comprising administering to a patient in need thereof a  
10 therapeutically effective amount of a compound of claim  
1.

23. A method for treating disorders, comprising  
administering to a patient in need thereof a  
15 therapeutically effective amount of a compound of claim  
1, said disorders being selected from osteoarthritis,  
aneurism, fever, cardiovascular effects, Crohn's disease,  
congestive heart failure, autoimmune diseases, HIV-  
infection, HIV-associated dementia, psoriasis, idiopathic  
20 pulmonary fibrosis, transplant arteriosclerosis,  
physically- or chemically-induced brain trauma,  
inflammatory bowel disease, alveolitis, colitis, systemic  
lupus erythematosus, nephrotoxic serum nephritis,  
glomerularnephritis, asthma, multiple sclerosis,  
25 artherosclerosis, rheumatoid arthritis, restinosis, organ  
transplantation, and cancer.

24. The method for treating disorders, of claim 23,  
wherein said disorders being selected from psoriasis,  
30 idiopathic pulmonary fibrosis, transplant  
arteriosclerosis, physically- or chemically-induced brain  
trauma, inflammatory bowel disease, alveolitis, colitis,  
systemic lupus erythematosus, nephrotoxic serum  
nephritis, glomerularnephritis, asthma, multiple

sclerosis, arteriosclerosis, rheumatoid arthritis  
restinosis, organ transplantation, and cancer.

25. The method for treating disorders, of claim 24,  
5 wherein said disorders being selected from alveolitis,  
colitis, systemic lupus erythematosus, nephrotoxic serum  
nephritis, glomerularnephritis, asthma, multiple  
sclerosis, arteriosclerosis, rheumatoid arthritis  
restinosis, organ transplantation, and cancer.

10

26. The method for treating disorders, of claim 25,  
wherein said disorders being selected from asthma,  
multiple sclerosis, arteriosclerosis, and rheumatoid  
arthritis.

15

27. A method for treating inflammatory diseases,  
comprising administering to a patient in need thereof a  
therapeutically effective amount of a compound of claim  
1.

20

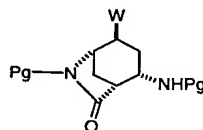
28. A method for modulation of CCR2 activity  
comprising administering to a patient in need thereof a  
therapeutically effective amount of a compound of claim  
1.

25

29. The method for treating disorders, of claim 25,  
wherein said disorders being selected from restinosis,  
organ transplantation, and cancer.

30

30. A compound of Formula (II)



(II)



wherein

W is selected from H, I, and Br;

5

Pg, at each occurrence, is independently selected from an amine protecting group.

31. The compound of claim 30, wherein

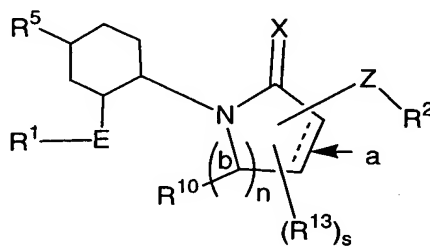
10

W is selected from H, I, and Br; and

Pg, at each occurrence, is independently selected from benzyloxycarbonyl (Cbz) and tert-butyloxycarbonyl (Boc).

15

32. A process for preparing a compound of Formula (Ia)



(Ia)

20 or salt or stereoisomer thereof: wherein

E is selected from -S(O)<sub>p</sub>CHRe-, -CHReNRe-, -C(O)-NRe-,  
-NReC(O)NRe-, -SO<sub>2</sub>-NRe-, and -NReSO<sub>2</sub>NRe-;

25 Re is independently selected from H and C<sub>1-3</sub> alkyl;

X is selected from O or S;

Z is selected from a bond,  $-\text{NR}^8\text{C}(\text{O})-$ ,  $-\text{NR}^8\text{C}(\text{S})-$ ,  
 $-\text{NR}^8\text{C}(\text{O})\text{NH}-$ ,  $-\text{NR}^8\text{C}(\text{S})\text{NH}-$ ,  $-\text{NR}^8\text{SO}_2-$ ,  $-\text{NR}^8\text{SO}_2\text{NH}-$ ,  
 $-\text{C}(\text{O})\text{NR}^8-$ ,  $-\text{OC}(\text{O})\text{NR}^8-$ ,  $-\text{NR}^8\text{C}(\text{O})\text{O}-$ ,  $-(\text{CR}^{15}\text{R}^{15})_1-$ ,  
 $-\text{CR}^{14}=\text{CR}^{14}-$ ,  $-\text{CR}^{15}\text{R}^{15}\text{C}(\text{O})-$ ,  $-\text{C}(\text{O})\text{CR}^{15}\text{R}^{15}-$ ,  
5  $\text{CR}^{15}\text{R}^{15}\text{C}(=\text{N}-\text{OR}^{16})-$ ,  $-\text{O}-\text{CR}^{14}\text{R}^{14}-$ ,  $-\text{CR}^{14}\text{R}^{14}-\text{O}-$ ,  $-\text{O}-$ ,  
 $-\text{NR}^9-$ ,  $-\text{NR}^9-\text{CR}^{14}\text{R}^{14}-$ ,  $-\text{CR}^{14}\text{R}^{14}-\text{NR}^9-$ ,  $-\text{S}(\text{O})_{\text{p}}-$ ,  $-\text{S}(\text{O})_{\text{p}}-$   
 $\text{CR}^{14}\text{R}^{14}-$ ,  $-\text{CR}^{14}\text{R}^{14}-\text{S}(\text{O})_{\text{p}}-$ , and  $-\text{S}(\text{O})_{\text{p}}-\text{NR}^9-$ ;

wherein neither Z nor  $\text{R}^{13}$  are connected to a carbon atom  
10 labeled (b);

bond (a) is a single or double bond;

alternatively, when n is equal to 2, two atoms labeled  
15 (b) may join through a double bond;

$\text{R}^1$  is selected from a  $\text{C}_{6-10}$  aryl group substituted with  
0-5  $\text{R}^6$  and a 5-10 membered heteroaryl system  
containing 1-4 heteroatoms selected from N, O, and  
20 S, substituted with 0-3  $\text{R}^6$ ;

$\text{R}^2$  is selected from a  $\text{C}_{6-10}$  aryl group substituted with  
0-5  $\text{R}^7$  and a 5-10 membered heteroaryl system  
containing 1-4 heteroatoms selected from N, O, and  
25 S, substituted with 0-3  $\text{R}^7$ ;

$\text{R}^5$ , at each occurrence, is independently selected from H,  
 $(\text{CRR})_{\text{r}}\text{OH}$ ,  $(\text{CRR})_{\text{r}}\text{SH}$ ,  $(\text{CRR})_{\text{r}}\text{OR}^{5\text{d}}$ ,  $(\text{CRR})_{\text{r}}\text{SR}^{5\text{d}}$ ,  
 $(\text{CRR})_{\text{r}}\text{NR}^{5\text{a}}\text{R}^{5\text{a}}$ ,  $(\text{CRR})_{\text{r}}\text{N}(\rightarrow\text{O})\text{R}^{5\text{a}}\text{R}^{5\text{a}}$ ,  $(\text{CRR})_{\text{r}}\text{NR}^{5\text{a}}\text{C}(\text{O})\text{R}^{5\text{b}}$ ,  
30  $(\text{CRR})_{\text{r}}\text{OC}(\text{O})\text{NR}^{5\text{a}}\text{R}^{5\text{a}}$ ,  $(\text{CRR})_{\text{r}}\text{NR}^{5\text{a}}\text{C}(\text{O})\text{OR}^{5\text{d}}$ ,  
 $(\text{CRR})_{\text{r}}\text{NR}^{5\text{a}}\text{C}(\text{O})\text{NR}^{5\text{a}}\text{R}^{5\text{a}}$ ,  $(\text{CRR})_{\text{r}}\text{NR}^{5\text{a}}\text{C}(\text{O})\text{H}$ ,  
 $(\text{CRR})_{\text{r}}\text{OC}(\text{O})\text{R}^{5\text{b}}$ ,  $(\text{CRR})_{\text{r}}\text{S}(\text{O})_{\text{p}}\text{R}^{5\text{b}}$ ,  $(\text{CRR})_{\text{r}}\text{S}(\text{O})_2\text{NR}^{5\text{a}}\text{R}^{5\text{a}}$ ,  
 $(\text{CRR})_{\text{r}}\text{NR}^{5\text{a}}\text{S}(\text{O})_2\text{R}^{5\text{b}}$ ,  $(\text{CRR})_{\text{r}}\text{NR}^{5\text{a}}\text{S}(\text{O})_2\text{NR}^{5\text{a}}\text{R}^{5\text{a}}$ , and a  
 $(\text{CRR})_{\text{r}}-5-10$  membered heterocyclic system containing

1-4 heteroatoms selected from N, O, and S,  
substituted with 0-2 R<sup>5c</sup>;

5 R<sup>5a</sup>, at each occurrence, is independently selected from H,  
methyl substituted with 0-1 R<sup>5g</sup>, C<sub>2-6</sub> alkyl  
substituted with 0-2 R<sup>5e</sup>, C<sub>3-8</sub> alkenyl substituted  
with 0-2 R<sup>5e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>5e</sup>,  
a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub> carbocyclic residue substituted with  
0-5 R<sup>5e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-10 membered heterocyclic  
10 system containing 1-4 heteroatoms selected from N,  
O, and S, substituted with 0-3 R<sup>5e</sup>;

R<sup>5b</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl  
substituted with 0-3 R<sup>5e</sup>, C<sub>3-8</sub> alkenyl substituted  
15 with 0-2 R<sup>5e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>5e</sup>,  
a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue substituted with  
0-2 R<sup>5e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic  
system containing 1-4 heteroatoms selected from N,  
O, and S, substituted with 0-3 R<sup>5e</sup>;

20 R<sup>5c</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub>  
alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> cycloalkyl, Cl, Br,  
I, F, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, NO<sub>2</sub>, CN, (CH<sub>2</sub>)<sub>r</sub>NR<sup>5f</sup>R<sup>5f</sup>, (CH<sub>2</sub>)<sub>r</sub>OH,  
(CH<sub>2</sub>)<sub>r</sub>OC<sub>1-4</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>SC<sub>1-4</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>C(O)OH,  
25 (CH<sub>2</sub>)<sub>r</sub>C(O)R<sup>5b</sup>, (CH<sub>2</sub>)<sub>r</sub>C(O)NR<sup>5f</sup>R<sup>5f</sup>, (CH<sub>2</sub>)<sub>r</sub>OC(O)NR<sup>5f</sup>R<sup>5f</sup>,  
(CH<sub>2</sub>)<sub>r</sub>NR<sup>5f</sup>C(O)R<sup>5b</sup>, (CH<sub>2</sub>)<sub>r</sub>C(O)OC<sub>1-4</sub> alkyl,  
(CH<sub>2</sub>)<sub>r</sub>NR<sup>5f</sup>C(O)OC<sub>1-4</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>OC(O)R<sup>5b</sup>,  
(CH<sub>2</sub>)<sub>r</sub>C(=NR<sup>5f</sup>)NR<sup>5f</sup>R<sup>5f</sup>, (CH<sub>2</sub>)<sub>r</sub>S(O)<sub>p</sub>R<sup>5b</sup>,  
(CH<sub>2</sub>)<sub>r</sub>NHC(=NR<sup>5f</sup>)NR<sup>5f</sup>R<sup>5f</sup>, (CH<sub>2</sub>)<sub>r</sub>S(O)<sub>2</sub>NR<sup>5f</sup>R<sup>5f</sup>,  
30 (CH<sub>2</sub>)<sub>r</sub>NR<sup>5f</sup>S(O)<sub>2</sub>R<sup>5b</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl substituted with  
0-3 R<sup>5e</sup>;

R<sup>5d</sup>, at each occurrence, is selected from methyl, CF<sub>3</sub>,  
C<sub>2-6</sub> alkyl substituted with 0-2 R<sup>5e</sup>, C<sub>3-8</sub> alkenyl

substituted with 0-2 R<sup>5e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>5e</sup>, and a C<sub>3-10</sub> carbocyclic residue substituted with 0-3 R<sup>5e</sup>;

- 5 R<sup>5e</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, C<sub>3-6</sub> cycloalkyl, Cl, F, Br, I, CN, NO<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>OC<sub>1-5</sub> alkyl, OH, SH, (CH<sub>2</sub>)<sub>r</sub>SC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>NR<sup>5f</sup>R<sup>5f</sup>, and (CH<sub>2</sub>)<sub>r</sub>phenyl;
- 10 R<sup>5f</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl, and C<sub>3-6</sub> cycloalkyl;

R<sup>5g</sup> is independently selected from -C(O)R<sup>5b</sup>, -C(O)OR<sup>5d</sup>, -C(O)NR<sup>5f</sup>R<sup>5f</sup>, -CN, and (CH<sub>2</sub>)<sub>r</sub>phenyl;

15

R, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl substituted with R<sup>5e</sup>, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, and (CH<sub>2</sub>)<sub>r</sub>phenyl substituted with R<sup>5e</sup>;

20

R<sup>6</sup>, at each occurrence, is selected from C<sub>1-8</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>C<sub>3-6</sub> cycloalkyl, Cl, Br, I, F, NO<sub>2</sub>, CN, (CR'R')<sub>r</sub>NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>OH, (CR'R')<sub>r</sub>O(CR'R')<sub>r</sub>R<sup>6d</sup>, (CR'R')<sub>r</sub>SH, (CR'R')<sub>r</sub>C(O)H, (CR'R')<sub>r</sub>S(CR'R')<sub>r</sub>R<sup>6d</sup>, (CR'R')<sub>r</sub>SC(O)(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>C(O)OH, (CR'R')<sub>r</sub>C(O)(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>C(O)NR<sup>6a</sup>R<sup>6a</sup>, (CR'R')<sub>r</sub>NR<sup>6f</sup>C(O)(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>C(O)O(CR'R')<sub>r</sub>R<sup>6d</sup>, (CR'R')<sub>r</sub>OC(O)(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>OC(O)NR<sup>6a</sup>(CR'R')<sub>r</sub>R<sup>6d</sup>, (CR'R')<sub>r</sub>NR<sup>6a</sup>C(O)NR<sup>6a</sup>(CR'R')<sub>r</sub>R<sup>6d</sup>, (CR'R')<sub>r</sub>NR<sup>6a</sup>C(S)NR<sup>6a</sup>(CR'R')<sub>r</sub>R<sup>6d</sup>, (CR'R')<sub>r</sub>NR<sup>6f</sup>C(O)O(CR'R')<sub>r</sub>R<sup>6b</sup>, (CR'R')<sub>r</sub>C(=NR<sup>6f</sup>)NR<sup>6a</sup>R<sup>6a</sup>,

30

- $(\text{CR}'\text{R}')_r\text{NHC}(=\text{NR}^{6f})\text{NR}^{6f}\text{R}^{6f}$ ,  $(\text{CR}'\text{R}')_r\text{S}(\text{O})_p(\text{CR}'\text{R}')_r\text{R}^{6b}$ ,  
 $(\text{CR}'\text{R}')_r\text{S}(\text{O})_2\text{NR}^{6a}\text{R}^{6a}$ ,  $(\text{CR}'\text{R}')_r\text{NR}^{6f}\text{S}(\text{O})_2\text{NR}^{6a}\text{R}^{6a}$ ,  
 $(\text{CR}'\text{R}')_r\text{NR}^{6f}\text{S}(\text{O})_2(\text{CR}'\text{R}')_r\text{R}^{6b}$ ,  $\text{C}_{1-6}$  haloalkyl,  $\text{C}_{2-8}$   
 alkenyl substituted with 0-3  $\text{R}'$ ,  $\text{C}_{2-8}$  alkynyl  
 5 substituted with 0-3  $\text{R}'$ ,  $(\text{CR}'\text{R}')_r\text{phenyl}$  substituted  
 with 0-3  $\text{R}^{6e}$ , and a  $(\text{CH}_2)_r\text{-5-6}$  membered heterocyclic  
 system containing 1-2 heteroatoms selected from N,  
 O, and S, substituted with 0-2  $\text{R}^{6e}$ ;
- 10 alternatively, two  $\text{R}^6$  on adjacent atoms on  $\text{R}^1$  may join to  
 form a cyclic acetal;
- $\text{R}^{6a}$ , at each occurrence, is selected from H, methyl  
 substituted with 0-1  $\text{R}^{6g}$ ,  $\text{C}_{2-6}$  alkyl substituted with  
 15 0-2  $\text{R}^{6e}$ ,  $\text{C}_{3-8}$  alkenyl substituted with 0-2  $\text{R}^{6e}$ ,  $\text{C}_{3-8}$   
 alkynyl substituted with 0-2  $\text{R}^{6e}$ , a  $(\text{CH}_2)_r\text{-C}_{3-10}$   
 carbocyclic residue substituted with 0-5  $\text{R}^{6e}$ , and a  
 $(\text{CH}_2)_r\text{-5-10}$  membered heterocyclic system containing  
 1-4 heteroatoms selected from N, O, and S,  
 20 substituted with 0-2  $\text{R}^{6e}$ ;
- $\text{R}^{6b}$ , at each occurrence, is selected from H,  $\text{C}_{1-6}$  alkyl  
 substituted with 0-2  $\text{R}^{6e}$ ,  $\text{C}_{3-8}$  alkenyl substituted  
 with 0-2  $\text{R}^{6e}$ ,  $\text{C}_{3-8}$  alkynyl substituted with 0-2  $\text{R}^{6e}$ ,  
 25 a  $(\text{CH}_2)_r\text{C}_{3-6}$  carbocyclic residue substituted with 0-3  
 $\text{R}^{6e}$ , and a  $(\text{CH}_2)_r\text{-5-6}$  membered heterocyclic system  
 containing 1-4 heteroatoms selected from N, O, and  
 S, substituted with 0-2  $\text{R}^{6e}$ ;
- 30  $\text{R}^{6d}$ , at each occurrence, is selected from  $\text{C}_{3-8}$  alkenyl  
 substituted with 0-2  $\text{R}^{6e}$ ,  $\text{C}_{3-8}$  alkynyl substituted  
 with 0-2  $\text{R}^{6e}$ , methyl,  $\text{CF}_3$ ,  $\text{C}_{2-6}$  alkyl substituted  
 with 0-3  $\text{R}^{6e}$ ,  $\text{C}_{2-4}$  haloalkyl, a  $(\text{CH}_2)_r\text{-C}_{3-10}$   
 carbocyclic residue substituted with 0-3  $\text{R}^{6e}$ , and a

$(\text{CH}_2)_r$ -5-6 membered heterocyclic system containing  
1-4 heteroatoms selected from N, O, and S,  
substituted with 0-3  $\text{R}^{6e}$ ;

- 5  $\text{R}^{6e}$ , at each occurrence, is selected from  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-8}$   
alkenyl,  $\text{C}_{2-8}$  alkynyl,  $(\text{CH}_2)_r\text{C}_{3-6}$  cycloalkyl, Cl, F,  
Br, I, CN,  $\text{NO}_2$ ,  $(\text{CF}_2)_r\text{CF}_3$ ,  $(\text{CH}_2)_r\text{OC}_{1-5}$  alkyl, OH, SH,  
 $(\text{CH}_2)_r\text{SC}_{1-5}$  alkyl,  $(\text{CH}_2)_r\text{NR}^{6f}\text{R}^{6f}$ , and  $(\text{CH}_2)_r\text{phenyl}$ ;
- 10  $\text{R}^{6f}$ , at each occurrence, is selected from H,  $\text{C}_{1-5}$  alkyl,  
and  $\text{C}_{3-6}$  cycloalkyl, and phenyl;

$\text{R}^{6g}$  is independently selected from  $-\text{C}(\text{O})\text{R}^{6b}$ ,  $-\text{C}(\text{O})\text{OR}^{6d}$ ,  
 $-\text{C}(\text{O})\text{NR}^{6f}\text{R}^{6f}$ , and  $(\text{CH}_2)_r\text{phenyl}$ ;

15

- $\text{R}^7$ , at each occurrence, is selected from  $\text{C}_{1-8}$  alkyl,  $\text{C}_{2-8}$   
alkenyl,  $\text{C}_{2-8}$  alkynyl,  $(\text{CH}_2)_r\text{C}_{3-6}$  cycloalkyl, Cl, Br,  
I, F,  $\text{NO}_2$ , CN,  $(\text{CR}'\text{R}')_r\text{NR}^{7a}\text{R}^{7a}$ ,  $(\text{CR}'\text{R}')_r\text{OH}$ ,  
 $(\text{CR}'\text{R}')_r\text{O}(\text{CR}'\text{R}')_r\text{R}^{7d}$ ,  $(\text{CR}'\text{R}')_r\text{SH}$ ,  $(\text{CR}'\text{R}')_r\text{C}(\text{O})\text{H}$ ,  
20  $(\text{CR}'\text{R}')_r\text{S}(\text{CR}'\text{R}')_r\text{R}^{7d}$ ,  $(\text{CR}'\text{R}')_r\text{C}(\text{O})\text{OH}$ ,  
 $(\text{CR}'\text{R}')_r\text{C}(\text{O})(\text{CR}'\text{R}')_r\text{R}^{7b}$ ,  $(\text{CR}'\text{R}')_r\text{C}(\text{O})\text{NR}^{7a}\text{R}^{7a}$ ,  
 $(\text{CR}'\text{R}')_r\text{NR}^{7f}\text{C}(\text{O})(\text{CR}'\text{R}')_r\text{R}^{7b}$ ,  $(\text{CR}'\text{R}')_r\text{C}(\text{O})\text{O}(\text{CR}'\text{R}')_r\text{R}^{7d}$ ,  
 $(\text{CR}'\text{R}')_r\text{OC}(\text{O})(\text{CR}'\text{R}')_r\text{R}^{7b}$ ,  
 $(\text{CR}'\text{R}')_r\text{OC}(\text{O})\text{NR}^{7a}(\text{CR}'\text{R}')_r\text{R}^{7a}$ ,  
25  $(\text{CR}'\text{R}')_r\text{NR}^{7a}\text{C}(\text{O})\text{NR}^{7a}(\text{CR}'\text{R}')_r\text{R}^{7a}$ ,  
 $(\text{CR}'\text{R}')_r\text{NR}^{7f}\text{C}(\text{O})\text{O}(\text{CR}'\text{R}')_r\text{R}^{7d}$ ,  $(\text{CR}'\text{R}')_r\text{C}(=\text{NR}^{7f})\text{NR}^{7a}\text{R}^{7a}$ ,  
 $(\text{CR}'\text{R}')_r\text{NHC}(=\text{NR}^{7f})\text{NR}^{7f}\text{R}^{7f}$ ,  $(\text{CR}'\text{R}')_r\text{S}(\text{O})_p(\text{CR}'\text{R}')_r\text{R}^{7b}$ ,  
 $(\text{CR}'\text{R}')_r\text{S}(\text{O})_2\text{NR}^{7a}\text{R}^{7a}$ ,  $(\text{CR}'\text{R}')_r\text{NR}^{7a}\text{S}(\text{O})_2\text{NR}^{7a}\text{R}^{7a}$ ,  
 $(\text{CR}'\text{R}')_r\text{NR}^{7f}\text{S}(\text{O})_2(\text{CR}'\text{R}')_r\text{R}^{7b}$ ,  $\text{C}_{1-6}$  haloalkyl,  $\text{C}_{2-8}$   
30 alkenyl substituted with 0-3  $\text{R}'$ ,  $\text{C}_{2-8}$  alkynyl  
substituted with 0-3  $\text{R}'$ ,  $(\text{CR}'\text{R}')_r\text{C}_{3-10}$  carbocyclic  
residue and  $(\text{CR}'\text{R}')_r\text{phenyl}$  substituted with 0-3  $\text{R}^{7e}$ ;

alternatively, two R<sup>7</sup> on adjacent atoms on R<sup>2</sup> may join to form a cyclic acetal;

5 R<sup>7a</sup>, at each occurrence, is independently selected from H, methyl substituted with 0-1 R<sup>7g</sup>, C<sub>2-6</sub> alkyl substituted with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkenyl substituted with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>7e</sup>, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub> carbocyclic residue substituted with 0-5 R<sup>7e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-10 membered heterocyclic  
10 system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R<sup>7e</sup>;

R<sup>7b</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl substituted with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkenyl substituted with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>7e</sup>,  
15 a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> carbocyclic residue substituted with 0-3 R<sup>7e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R<sup>7e</sup>;

20 R<sup>7d</sup>, at each occurrence, is selected from C<sub>3-8</sub> alkenyl substituted with 0-2 R<sup>7e</sup>, C<sub>3-8</sub> alkynyl substituted with 0-2 R<sup>7e</sup>, methyl, CF<sub>3</sub>, C<sub>2-4</sub> haloalkyl, C<sub>2-6</sub> alkyl substituted with 0-3 R<sup>7e</sup>, a (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-10</sub> carbocyclic  
25 residue substituted with 0-3 R<sup>7e</sup>, and a (CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R<sup>7e</sup>;

30 R<sup>7e</sup>, at each occurrence, is selected from C<sub>1-6</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, (CH<sub>2</sub>)<sub>r</sub>-C<sub>3-6</sub> cycloalkyl, Cl, F, Br, I, CN, NO<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>-CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>-OC<sub>1-5</sub> alkyl, OH, SH, C(O)OC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>-SC<sub>1-5</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>-NR<sup>7f</sup>R<sup>7f</sup>, and (CH<sub>2</sub>)<sub>r</sub>-phenyl;

$R^{7f}$ , at each occurrence, is selected from H,  $C_{1-5}$  alkyl, and  $C_{3-6}$  cycloalkyl, and phenyl;

- 5  $R^{7g}$  is independently selected from  $-C(O)R^{7b}$ ,  $-C(O)OR^{7d}$ ,  $-C(O)NR^{7f}R^{7f}$ , and  $(CH_2)_r$ phenyl;

- $R'$ , at each occurrence, is selected from H,  $C_{1-6}$  alkyl substituted with  $R^{6e}$ ,  $C_{2-8}$  alkenyl,  $C_{2-8}$  alkynyl,  
10  $(CH_2)_rC_{3-6}$  cycloalkyl, and  $(CH_2)_r$ phenyl substituted with  $R^{6e}$ ;

$R^8$  is selected from H,  $C_{1-4}$  alkyl, and  $C_{3-4}$  cycloalkyl;

- 15  $R^9$  is selected from H,  $C_{1-4}$  alkyl,  $C_{3-4}$  cycloalkyl,  $-C(O)H$ , and  $-C(O)-C_{1-4}$ alkyl;

- $R^{10}$  is independently selected from H, and  $C_{1-4}$ alkyl substituted with 0-1  $R^{10b}$ , alternatively, two  $R^{10}$   
20 form =O;

$R^{10b}$ , at each occurrence, is independently selected from  $-OH$ ,  $-SH$ ,  $-NR^{10c}R^{10c}$ ,  $-C(O)NR^{10c}R^{10c}$ , and  $-NHC(O)R^{10c}$ ;

- 25  $R^{10c}$  is selected from H,  $C_{1-4}$  alkyl and  $C_{3-6}$  cycloalkyl;

$R^{14}$ , at each occurrence, is independently selected from H and  $C_{1-4}$ alkyl;

- 30 alternatively, two  $R^{14}$ s, along with the carbon atom to which they are attached, join to form a  $C_{3-6}$  carbocyclic ring;



R<sup>15</sup>, at each occurrence, is independently selected from H, C<sub>1-4</sub>alkyl, OH, NH<sub>2</sub>, -O-C<sub>1-4</sub> alkyl, NR<sup>15a</sup>R<sup>15a</sup>, C(O)NR<sup>15a</sup>R<sup>15a</sup>, NR<sup>15a</sup>C(O)R<sup>15b</sup>, NR<sup>15a</sup>C(O)OR<sup>15d</sup>, OC(O)NR<sup>15a</sup>R<sup>15a</sup>, and (CHR)<sub>r</sub>C(O)OR<sup>15d</sup>;

5

alternatively, two R<sup>15</sup>s, along with the carbon atom or atoms to which they are attached, join to form a C<sub>3-6</sub> carbocyclic ring;

10 R<sup>15a</sup>, at each occurrence, is independently selected from H, and C<sub>1-4</sub> alkyl;

R<sup>15b</sup>, at each occurrence, is independently selected from C<sub>1-4</sub> alkyl, C<sub>3-6</sub> alkenyl, and C<sub>3-6</sub> alkynyl;

15

R<sup>15d</sup>, at each occurrence, is independently selected from C<sub>1-4</sub> alkyl, C<sub>3-6</sub> alkenyl, and C<sub>3-6</sub> alkynyl;

R<sup>16</sup> is selected from C<sub>1-4</sub> alkyl;

20

l is selected from 1, 2 and 3;

n is selected from 0, 1, 2, and 3;

25 p, at each occurrence, is independently selected from 0, 1, and 2;

q, at each occurrence, is independently selected from 1, 2, 3, and 4;

30

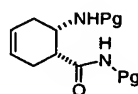
r, at each occurrence, is independently selected from 0, 1, 2, 3, and 4;

s is selected from 0 and 1; and

t, at each occurrence, is independently selected from 2,  
3, and 4;

5

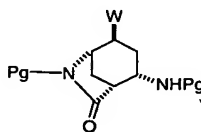
the steps comprising reacting a compound of Formula IV,



(IV)

10

with an electrophile and base to give a compound of  
Formula II;



(II)

wherein

15

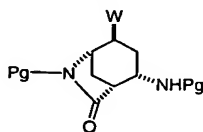
W is selected from H, I, and Br;

Pg, at each occurrence, is independently selected from an  
amine protecting group;

20

reacting a compound of Formula II to give the compound of  
Formula (Ia).

33. A process for preparing a compound of Formula (II)

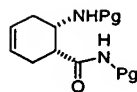


(II)

25

or salt or stereoisomer thereof,

comprising reacting a compound of Formula (IV)



(IV)

with an electrophile and a base,

5 wherein

W is selected from I and Br;

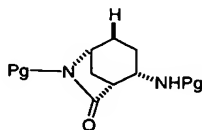
Pg, at each occurrence, is independently selected from an  
10 amine protecting group.

34. The process of claim 33 wherein

the electrophile is selected from iodine, bromine, N-  
15 bromo-succimide, and N-iodosuccinimide; and

the base is selected from n-butyl lithium, lithium  
diisopropylamide (LDA), sodium hydride, lithium  
bis(trimethylsilyl)amide, potassium  
20 bis(trimethylsilyl)amide, sodium bis(trimethylsilyl)-  
amide, and Li-Al(O-tButyl)<sub>4</sub>.

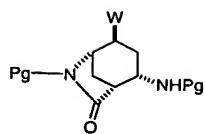
35. A process for preparing a compound of Formula (IIa)



(IIa)

25 or salt or stereoisomer thereof,

comprising reduction of a compound of Formula (II) with a  
reducing agent;



(II)

wherein W is selected from I and Br , and

Pg, at each occurrence, is independently selected from an  
 5 amine protecting group.

36. The process of claim 35, wherein the reducing agent  
 is selected from tris-(trimethylsilyl)silane, zinc metal,  
 tributyltin hydride and AIBN.

10